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SCHISTOSOMIASIS JAPONICA

Diagnosis and Treatment in American Soldiers

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FOLLOWING the invasion of Leyte, an island in the Philippines, on October 20, 1944, cases of schistosomiasis japonica began to appear among Army personnel. It is the purpose of this report to describe briefly the results of an investigation of 481 patients studied four to nine months after acquiring the disease. The dissemination of this information will enable patients from this and other hospitals who are being discharged from the Army and scattered throughout the country to obtain appropriate care in places where the disease is unknown. Although the results of this study are to be reported separately in considerable detail,[1] it is believed that the information acquired concerning diagnosis and treatment merits wider distribution. Since up to the present no snail capable of acting as an intermediate host for the parasite has been found in the United States,[2] it is not expected that the disease will be disseminated in this country. The problem therefore resolves itself into one of assuring proper care and follow-up for the small number of soldiers already infected.

THE ACUTE ILLNESS OVERSEAS

Several weeks after exposure, the patients developed chills, sweats, generalized malaise, lethargy, headache, anorexia, mild diarrhea and abdominal pain, with marked weight loss. Urticaria and jaundice were observed in some cases. Examination revealed a slightly enlarged and tender liver and occasionally an enlarged spleen. Leukocytosis with marked eosinophilia was usual. In some asymptomatic cases suspected of the disease because of eosinophilia, the ova of *Schistosoma japonicum* were found in the stools. In 8 of the 481 patients considered at this hospital to have had schistosomiasis japonica, there were weakness of the extremities and reflex abnormalities that followed an encephalomyelitis in the acute phase of the disease.

In about three fourths of the patients the ova of *Schistosoma japonicum* were found in the stools. Fuadin was given to almost all the patients treated overseas, the usual amount given being approximately 40 cc. In some cases a second course of the drug was given. Tartar emetic, in a concentration higher than that employed at this hospital, was used in a small number of cases.

THE DISEASE AS SEEN IN THE UNITED STATES

Four to nine months following their acute illness, patients were evacuated to this country for further study. On arrival at this hospital, they were convalescent and did not appear ill. The only abnormalities that appeared to have some specificity were recurrent cramps and tenderness in the upper abdomen. A slightly enlarged liver was felt in 10 per cent of the patients.

During the period of observation here, which lasted for three months or more, the patients tended to improve clinically whether or not their stools were demonstrated to contain ova. On discharge almost all the patients were free of signs and symptoms of the disease and had no disability preventing unlimited activity. They were advised, however, to have their stools examined every three months for a period of one year for reasons given below.

EXAMINATION OF STOOLS

The stools were examined over a period of at least two weeks initially and after two furloughs of thirty and twenty days, respectively. Patients untreated at this hospital because of repeatedly negative stools were released after an average of twenty-two stool examinations over a period averaging four months.

Methods

Stools were examined in all patients by multiple direct smears and in some by concentration methods. Although multiple direct smears detected the vast majority of positive stools, in a small number one or another of the sedimentation methods was necessary

for detection of the ova. When a modified gravity sedimentation method was made available,[3] it was found in a comparative study to add a significant number of positive results.[4]

In the direct smear method, a bit of mucus is taken from the outside of the stool, as being likeliest to contain eggs. This is mixed with a small amount of tap water and mounted under a coverslip. Search of the entire covered area is made through the low-power lens of the microscope, and any suspicious objects are examined under the high-dry lens. Eggs were in most cases readily distinguished under low power. Even under high power, the single laterally placed knoblike spine was rarely seen. Motion of the miracidia could be seen in viable eggs.

In the modified gravity sedimentation method of Barody,[3] approximately 5 gm. of feces is partially emulsified in 35 cc. of tap water by shaking in a 100-cc. test tube. The fluid is strained through a single layer of surgical gauze into a 30-cc. centrifuge tube and centrifuged at 1000 r.p.m. for one minute. The supernatant fluid is discarded and the sediment is resuspended in tap water. Centrifuging is repeated three or four times until the supernatant fluid is relatively clear. A portion of the final sediment is transferred to a slide, covered and examined microscopically.

Results

Thirty-one per cent of all patients admitted to this hospital with a diagnosis of schistosomiasis japonica had eggs in their stools, and the results of stool findings overseas combined with those obtained here proved conclusively that 80 per cent of these patients had schistosomiasis. In the remainder the clinical history was sufficiently characteristic to warrant little doubt of the diagnosis.

In approximately 10 per cent of the cases found to be positive here, the eggs were not found until the final follow-up period, when a minimum of twelve stools had been examined. In some cases, more than twenty stools were examined before ova were found.

An eosinophilia of 10 per cent or more was found in half the cases on admission here and was associated with the finding of ova in the stools two or three times more frequently than when the eosinophilia was less than 10 per cent. During the follow-up periods, however, an eosinophilia of more than 20 per cent was occasionally encountered even in the cases with repeatedly negative stools. Although not of specific diagnostic value in schistosomiasis because of its presence in other parasitic infections, a persistent eosinophilia demands an even more meticulous search for schistosome eggs.

A variety of liver-function tests done on initial examination showed a 10 per cent incidence of mild impairment.[5] There was no apparent relation between these abnormalities and the stool findings.

Sigmoidoscopy was done routinely in the first 300 patients. Abnormalities were found in only 3 patients. Since the stools of these patients contained ova on direct examination, this procedure was not helpful in making the diagnosis. Barium enemas in 50 cases were normal.

Of the stools of 463 patients evacuated with a diagnosis of schistosomiasis japonica, those of 146 (31.5 per cent) showed one hundred and seventy-eight infections with seven species of pathogenic intestinal parasites. The incidence of infection in these 146 patients was as follows: hookworm, 16.4 per cent; trichocephalus, 11.4 per cent; *endamoeba histolytica*, 3.5 per cent; *Ascaris lumbricoides*, 3.2 per cent; Strongyloides, 2.2 per cent; *Hymenolepis nana*, 1.1 per cent; and *Giardia lamblia*, 0.6 per cent.

Treatment

The incidence of the failure of treatment as judged by the finding of positive stools in patients treated overseas was found to be definitely lower with tartar emetic than with fuadin. Treatments with these two drugs at this hospital were also compared.

Fuadin

Fuadin, a trivalent antimony compound, was given in 6.3 per cent solution intramuscularly. Initial doses of 1.5, 3.5 and 5.0 cc. were given on successive days, followed by injections of 5.0 cc. every other day until a total of 65 cc. (0.57 gm. antimony) had been given, which required twenty-five days.[6]

Commercial Tartar Emetic

Commercial tartar emetic, also a trivalent antimony compound was given intravenously in the form of a 0.5 per cent solution in 5 per cent dextrose in normal saline solution at a maximum rate of 8 cc. a minute. The patient was required to lie down during the injection and for one hour after it. The drug was given every other day. The initial dose was 8 cc.; this was increased by 4 cc. with each dose until a level of 24 cc. was reached. Thereafter 24 cc. was given every other day until a total of 320 cc. (0.58 gm. of antimony) had been given, which required twenty-nine days.

Freshly Prepared Tartar Emetic

Freshly prepared tartar emetic was used as follows. Sufficient potassium and antimony tartrate was accurately weighed with a sterile technic to make a solution of 0.5 per cent in 5 per cent dextrose in normal saline solution. After the solution was prepared, it was heated in a boiling hot-water bath for five minutes and allowed to cool prior to administration. The solution was injected at the same rate and in the same amounts as was the commercial tartar emetic.

Evidence of Toxicity

Judging by the literature[7] and by certain reports from the Pacific,[8,9] toxic reactions due to intravenous tartar emetic may be of sufficient severity to pre-

clude its use. Much of this result may be due to too rapid injections or too high a concentration of the solution used. This conclusion is based on the insignificance of toxic reactions found in this study under the conditions outlined below.

With a dilute solution (0.5 per cent) and a slow rate of injection (8 cc. a minute), reactions sufficiently severe to justify stopping the drug were encountered in only 2 of the 102 patients treated with more than two thousand injections and carefully observed for evidence of reaction. Seventy-one per cent at one time or another developed a transient hacking cough. Nausea, occasionally associated with vomiting, appeared in 15 per cent. In most cases, the nausea could be diminished by having the patient suck a piece of lemon during the injection. The most striking toxic reaction was a transient sense of soreness, usually in the region of the shoulders, which appeared eight to twelve hours after the injection in 75 per cent of the cases. It did not prevent the patients from being ambulatory.

In all the patients treated with tartar emetic and in half of those treated with fuadin, there appeared a diminution in the size of the T waves in one or more leads of the electrocardiograms, with a complete inversion in some cases.[10] On casual examination these changes were like those seen in coronary thrombosis or pericarditis. With cessation of therapy, the T waves returned to normal. These changes were never associated with any clinical signs or symptoms of cardiac disease, and the drug was not stopped.

Some evidence has been obtained that antimony causes a minor transient impairment of liver function.[5] It is therefore suggested that in patients who require repeated treatment with antimony compounds, tests of liver function should be performed before, during and after the administration of therapy to determine whether there is any cumulative toxic effect.

No deleterious effect of antimony was noted in the urine or in the cellular constitutents of the blood.

Results

One hundred patients with ova of *S. japonicum* in the stools were treated with either fuadin or tartar emetic. The cases were alternated without regard to overseas therapy or to the patients' condition overseas or on arrival here. Additional patients were treated with longer courses of fuadin (105 cc.) and tartar emetic (416 cc.) at the same individual dose level. These patients are now being followed at another hospital.

After the completion of treatment, the patients were sent on a thirty-day furlough. On their return, follow-up studies were begun. An average of nineteen stools were examined over an average period of three and a half months following treatment before therapy was considered successful. Any patient whose stool was found to be positive at any time during the follow-up period was given the same course of treatment again and was similarly followed.

The rate of apparent cure (negative stools) in the tartar emetic group was 81 per cent, whereas that for the fuadin group was 18 per cent. In addition, of the 16 cases treated twice with fuadin at this hospital because of continued positive stools and followed for a short period of time, 69 per cent had positive stools for the third time.

Discussion

Schistosomiasis japonica as encountered in these patients offered a unique group for study. The usual textbook picture of this illness is based on the cases in which there has been repeated exposure over a period of years, whereas in this series the maximum length of exposure was only a few months. Furthermore, these patients were healthy soldiers who were given the advantages of prompt treatment.

The most frequent complication in the often exposed native population, owing to the deposition of the eggs, is said to be hepatomegaly and splenomegaly.[7] In the present series there was little evidence of such changes. Recurrent epigastric pain and tenderness appeared to be the most frequent symptom after the acute phase had subsided, but on discharge there was no evident disability. Whether definite liver disease may develop later if ova continue to be produced is not known. Asymptomatic infections also occurred. Certainly, the possibility should be kept in mind in all persons who were on the east coast of Leyte or in other endemic areas.[6]

Frequent stool examinations by more than one method are required to demonstrate the eggs in the stools. From these studies it is obvious that an occasional observation is insufficient. It is only by repeated stool examinations with multiple methods that eggs will be demonstrated, their discovery leading to the institution of therapy.

Treatment at this hospital with tartar emetic showed better results than did that with fuadin. Furthermore, the toxic symptoms of tartar emetic were for the most part mild. Since, however, the sole criterion of cure is the absence of eggs in the stools, no final conclusion can be drawn until these cases have been followed for many years. Our arbitrary recommendation of one year of follow-up may require alteration in the light of continuing collection of data.

Many of the soldiers showed anxiety about the possibility of developing disability at a later date. Intelligent reassurance can be based only on the taking of steps to guarantee them adequate re-examination and treatment in both the Army and civilian life. It is the purpose of this paper to call attention to this need.

Summary and Conclusions

Four hundred and eighty-one cases of schistosomiasis japonica acquired on Leyte, an island in

the Philippines, were studied at an Army general hospital in the United States.

Recurrent epigastric cramps and tenderness were the most frequent complaints on admission, but in almost all cases these had disappeared by the time of discharge.

Repeated stool examinations by more than one method were necessary to demonstrate the eggs of *Schistosoma japonicum*. A persistent eosinophilia was suggestive but not diagnostic of continued activity of the disease.

On the basis of comparable series, treatment with tartar emetic was found to be much more effective than that with fuadin. Significant toxic reactions with tartar emetic were rare.

It is urged that stool examinations be done repeatedly and by multiple methods on men who have been exposed to this disease so that treatment may be instituted if ova are found.

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WARTIME ACTIVITIES OF THE ARMY MEDICAL DEPARTMENT*

Major General Norman T. Kirk†

IT IS a distinct privilege to be present at this annual meeting of the Tufts Medical Alumni Association. I look back with pleasant memories to about a year ago when I was present at the commissioning exercises of the graduating class of Tufts College Medical School and also those of Harvard and Boston universities. I thoroughly enjoyed renewing old acquaintances and making new friends on that occasion, and I am happy to be with you again tonight.

I am aware of the great contribution that the Tufts Medical Alumni Association and the Tufts College Medical School have made in this war. Some of you may not realize just how close my contact is with your institutions. The office on my immediate left is occupied by the deputy surgeon general, who is Brigadier General Raymond W. Bliss, a Tufts alumnus of the Class of 1910, and the office on my immediate right is that of the executive officer, Colonel Robert J. Carpenter, a Tuft alumnus of the Class of 1914. With an enthusiastic and loyal Tufts alumnus on either side, I think you can understand how I happen to be fairly well informed on your activities.

Tufts College Medical School has a rich heritage, dating back for over half a century, of providing New England and other sections of the country with high-type general practitioners. You have followed a policy of keeping in close touch with your alumni to see that they have kept abreast of modern practices. You have not overlooked the specialties, of course, but you have particularly stressed a program of developing to the highest professional standards your training of the general practitioner. In this day of specialization I am glad to see that your institution has not overlooked the fact that there is still a definite need for general practitioners in the rural sections.

I realize that everyone in this audience has played an important part in recent years, whether he served in uniform or remained to do the vitally necessary tasks in civilian practice or as part of the staff of Tufts College Medical School. You have contributed more than your share, and I think that you will be interested in hearing something of the overall story of the Army Medical Department's activities in the war. Now that it is over, I can give you a more intimate glimpse into what was done by this department since the start of the emergency.

You know that we had to start practically from scratch. In the Regular Army there were only about 1200 medical officers. In planning an organization geared to the medical needs of an army of 8,000,000, you can see what they meant. Largely because of the foresight and loyalty of professional men of your type, we had a reserve that helped us bring the strength of the Medical Corps to approximately 47,000 at the peak of the war. In addition, there were 15,000 officers in the Dental Corps, 2000 in the Veterinary Corps, 2000 in the Sanitary Corps, 61 in the Pharmacy Corps and 18,700 in the Medical Administrative Corps. The total number of nurses reached approximately 57,000, and there were 535,000 enlisted men trained as medical-aid men, technicians, litter bearers, ambulance drivers, clerks and so forth. The entire Medical Department had to be expanded from a skeleton organization into a full-blown medical machine, which did the biggest job ever performed by American medicine.

*An address delivered at the annual meeting of Tufts Medical Alumni Association, Boston, April 10, 1946.

†Surgeon general, United States Army.

From September, 1943, to the present time there was shipped a total of 698,973 tons of medical supplies, kits, chests and other medical items. In normal times such an operation represents a big job. In wartime, with shortages of many items needed for the production of these supplies and the difficulties in getting the goods transported, the job was accomplished only by fighting every ton of equipment almost every mile of the way from the raw material to medical aid for a wounded man.

Penicillin is a good illustration of the problems that confronted us. Prior to 1943 the world had produced a total of only 1 pound of penicillin. Early in 1945 the original goal of 300,000,000,000 units a month, or 15 pounds a day, was passed. The original price of $20 a vial was cut to the present figure of approximately 76 cents.

Atabrine was another source of worry. The Allied Nations lost 95 per cent of the world's supply of quinine when the Japanese captured the Netherlands East Indies. Like penicillin, atabrine also introduced what seemed like insurmountable obstacles in the intricate process of manufacture. It takes 2½ tons of chemicals to make 100 pounds of atabrine, a ratio of 30:1. On the surrender of Corregidor there were 35,000,000 tablets on hand and a yearly manufacturing capacity of 227,000,000 tablets. Through heavy pressure from the Medical Department production was boosted so that 3,500,000,000 tablets were produced in 1944, with the cost brought down from $24 per 1000 tablets in 1940 to $3 in 1944.

Blood plasma is an interesting item from a supply standpoint. The processing of blood plasma began in February, 1941. Procurement averaged approximately 140,000 units of 250 cc. per month, with an all-time high of 178,000 in October, 1944. Shipments of whole blood to Europe started in August, 1944, and continued until May, 1945, with a total shipment of 206,000 pints of Group O blood. To the Pacific, 177,784 pints were flown.

It was through the success of our operations in supply and personnel that we were able to staff, equip and maintain the system of Army hospitals. Overseas in all theaters there were 217 general, 196 station, 99 field, 91 evacuation and 73 portable surgical hospitals. Including convalescent hospitals and centers, there was a total of 692 hospitals overseas at the peak of operations. There were 65 general and 13 convalescent hospitals in the Zone of the Interior. During the war 15,000,000 patients were admitted to Army hospitals for treatment. The peak of the world-wide total load was 544,000 in April, 1945. The peak in Army hospitals in this country was 312,000 in August, 1945.

The American Army in this war was the healthiest in the world. The program of preventive medicine was an important factor in this record. Through the development and use of toxoids and vaccines, fear of tetanus, yellow fever and typhus became a thing of the past. There were no deaths from these diseases among American soldiers who were inoculated against them.

Malaria at one time incapacitated ten times as many soldiers as did Japanese bullets. Through proper control measures malaria was cut to one fourth its incidence in the early days of the war in the Pacific. Atabrine proved even more satisfactory than quinine. It serves as a suppressive just as quinine does, and also cures the malignant form of disease known as falciparum malaria. The part DDT played in the battle against disease was, of course, a major one. In my tours to overseas theaters I have seen islands, such as Saipan, where there were no traces of mosquitoes or flies as a result of the spraying of DDT from airplanes.

Preventive measures also played a large part in cutting down casualties in the Air Force. As air surgeon of the Eighth Air Force, Brigadier General Malcolm C. Grow worked out a system of rest camps, the spacing of missions farther apart and the establishment of a definite number of missions that when completed would end the flyer's tour of duty in that theater. These antifatigue measures proved highly effective in combating this problem among flyers.

To be certain that aviators had sufficient oxygen they were given courses of instruction in handling personal equipment, and "personal officers" were appointed to see that all missions were started with equipment in proper order. Heaters were developed to cut down the freezing of oxygen masks. These same officers checked clothing and equipment to guard against frostbite and instructed flyers how to prevent it. Engineers were instructed to keep the waist windows in the fuselage closed.

The field of medicine has also proved rich in results in this war. The death rate from disease was only 0.6 per 1000 men per year, as against 16.5 in the last war. The pneumonia rate was cut from 24 in the last war to 0.6, and that of meningitis was lowered from 38 to 4. Days lost due to venereal disease amounted to 47 per case in 1937, whereas last year the days lost per case totaled only 5.

Great advances were made in the adaptation of civilian to military surgery in this war, and improvements in both will be noted in the future from the facts that were learned. A great deal is owed to Colonel E. D. Churchill, surgical consultant in the Mediterranean Theater, for his development and standardization of wound management and resuscitation.

Surgical care has been divided into three echelons. The initial or primary echelon is in forward hospitals, where the wound is thoroughly débrided, left open, immobilized by plaster or splints and made ready for transportation to fixed hospitals in the rear. Resuscitation is necessary at this echelon of treatment. Most of these patients are in shock, and many have lost much blood. Plasma prevented

the loss of many lives after injury and previous to arrival at a hospital for surgery. It was soon demonstrated that plasma alone was not sufficient to permit life-saving surgery and must be supplemented by whole blood.

In the second echelon, intermediate or reparative surgery is carried on at the fixed hospital in the rear. Here, plaster and splints are removed, secondary closure is accomplished by plastic procedures or by skin grafts, and fractures of long bones are placed in suspension traction until consolidated and then fixed in plaster for transportation to the Zone of the Interior. Soft-tissue wounds heal much earlier under these procedures, and the soldier is returned to duty in the theater in a much shorter period of time. Compound fractures are converted into simple fractures, and the patients arrive home without osteomyelitis and with advanced union. Patients with colostomies that were performed as a life-saving measure when initial surgery was done are prepared for evacuation to the Zone of the Interior or the colostomy is closed in the theater. Thoracotomy for the removal of blood clot or foreign bodies becomes routine, and many of these patients return to duty in the theater instead of returning home with a drainage tube in the chest, with chronic empyema and marked loss of weight, and requiring extended hospitalization. Penicillin and sulfonamides aid materially in the prevention and control of infection, but they are adjuncts only to good surgery.

The third echelon is definitive or reconstructive surgery — mainly practiced in the Zone of the Interior and at times in the Zone of Communications. Here plastic procedures on skin, nerve, bone and vessels and other procedures are carried on to correct the defect, mobilize joints and prepare the patient for return to the Army or to civil life.

Surgery was an important factor in the following results, which will be of interest to you. Of 598,000 soldiers wounded in this war, approximately 96 per cent who reached Army hospitals lived, 26,600 dying of wounds; 376,000 were returned to duty in the theater; and an additional 55,200 were returned to duty in the United States. One hundred and ten thousand were returned to civilian life with a certificate of disability discharge. There are approximately 30,200 of these patients still receiving treatment in general hospitals here at home. These sick and wounded soldiers received the best medical care as a result of the system of specialized centers that the Army established in general hospitals. There were not enough specialists, so the Army brought the patients to the specialists. The following centers were established for specialized care: seven amputation centers, nineteen neurosurgery centers, five thoracic-surgery centers, eight plastic-surgery centers, two ophthalmologic-surgery and blind centers, three deaf centers, nine deep x-ray-therapy centers, three radium-therapy centers, three vascular centers, nineteen neurology centers, two arthritis centers, seven centers for syphilis of the central nervous system, two tuberculosis centers, two rheumatic-fever centers and two tropical-disease centers.

An example of how this specialized-center system worked out is afforded in the treatment of paraplegic patients. They are small in numbers, — only about 1400 in all — but the Army has devoted the same amount of effort to helping them as in the case of patients in larger groups. In fact, the results in these cases have surpassed anything in the previous history of neurosurgery and constitute a tribute to the professional competence of the Army doctors in this war. Until this program was instituted, men with spinal-cord injuries and resulting paralysis were regarded as hopeless invalids and, I fear, were treated as such. This attitude has been completely reversed by the Army Medical Corps, which met the problem with all the resources of the profession.

Prompt and skilled surgery was the first step in the treatment of these cases. Nutritionists and dietitians helped to restore underweight patients, who were evacuated to one of the nineteen neurosurgical centers. The next phase of treatment was largely urologic, and a urologist was in constant attendance. Decubitus ulcers were closed by surgery, either by skin grafting or by plastic procedures. Finally came the matter of ambulation. We did not deceive ourselves about this. Ambulation as you and I understand the term is beyond the capacity of all but the incomplete paraplegic patients, but ambulation in the sense of getting about with the aid of braces and crutches sufficiently well to care for oneself is a definite possibility in most patients with cord lesions at or below the tenth dorsal vertebra and is a more guarded possibility in cases with lesions below the second dorsal vertebra. In patients with lesions above this level ambulation is not possible, but a wheel-chair existence is. In other words, so far as this program was concerned, a bedridden patient was simply not conceived of. When a man reached a paraplegic center it was taken for granted that he would be out of bed promptly or at least as soon as certain physical deficiencies had been corrected and that he would attempt to walk with equal promptness. An unexplained improvement always occurs when these patients begin to move about. The surprising results we have realized in a majority of the cases have been against untold odds through the untiring and united efforts of neurosurgeons, plastic surgeons, orthopedic surgeons, urologists, internists, nutritionists, nurses, dietitians, physical therapists and hospital corpsmen. These results reflect the value of the specialized centers.

* * *

Most of what I have said refers to the work during the war, but I do not want to leave the impression

that our task has been finished. On March 1, 1946, there were 129,000 patients in Army hospitals, 60,000 of these being evacuees from overseas. You can see that we still have a sizable job on our hands. In addition, the Medical Department must lay its plans for the interim and postwar care of the Nation's soldiers. One important phase of this will be to secure a sufficient number of specialists for the Regular Army and Reserve Corps.

Here is where your organization can continue to help in the same grand way that you have in the past. Tufts Medical Alumni Association and Tufts College Medical School will continue to merit the deep appreciation of the Medical Department by giving their full support to the building of a strong Medical Reserve Corps. On behalf of the Army Medical Department, I express our sincere gratitude for what you have done, and judging by your members whom I know and the record of your past performances, I am certain that we can count on your unswerving and loyal support in our future plans for the type of Medical Reserve Corps that this country should and must have.

SCURVY*

A Survey of Two Hundred and Forty-One Cases

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ST. LOUIS, MISSOURI

SCURVY is still a reasonably frequent disease in pediatric practice. This is a disquieting fact that should cause concern to all responsible for the health of infants, inasmuch as the disease can so easily and effectively be prevented. The purpose of this report is to place on record the large number of cases seen in the Infants' and Children's hospitals during the last decade, to analyze the causes of inadequate intake of ascorbic acid and to suggest measures possibly leading to a decrease of the incidence of scurvy.

At least 241 clinically typical cases of scurvy were seen in these hospitals during the last ten years, according to the lists of the Record Library. The cases with insufficient data were not included in this report.

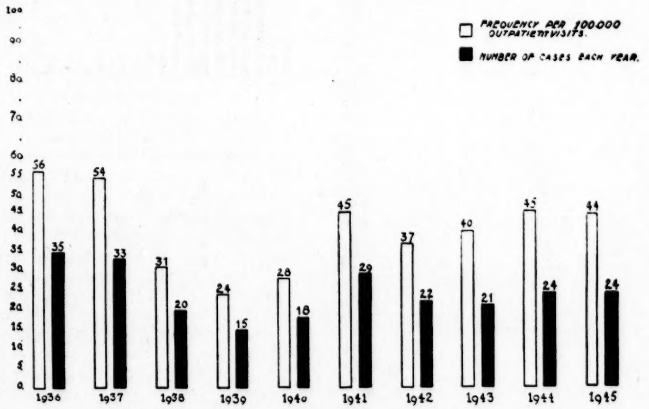

FIGURE 1. *Morbidity of Scurvy from 1936 to 1945.*

The criteria used in selecting the cases were twofold. First, all the selected cases had a history of inadequate vitamin C intake or some of the symptoms and signs characteristic of the disease, listed in Tables 1 and 2. Second, the diagnosis was verified in each case by roentgenograms and in a few cases by laboratory measurements or by the rapid therapeutic effect of vitamin C. The roentgen-ray evidence of the changes in the long bones included some

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or all of the following signs: Park's so-called "corner sign," cortical atrophy, ground-glass atrophy of the ends of the shaft, Fraenkel's so-called "white line" and in many cases evidence of swelling of the soft tissues of the lower extremities.

The incidence in males and females was approximately the same (Fig. 1).

The seasonal distribution is rather irregular in scurvy. It is sometimes said to be most frequent in winter and spring.[1] Park[2] observed that the greatest number of cases occur in September and October.

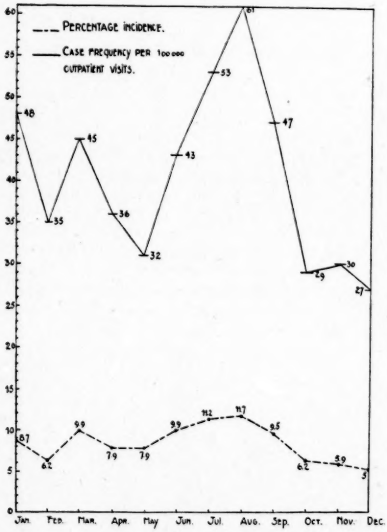

FIGURE 2. *Seasonal Incidence of Appearance of the First Symptom of Scurvy (241 cases).*

In the present series the incidence was high during the summer months and low in October, November and December (Fig. 2).

From Figure 3 it is clear that in the majority of the cases the first symptoms appear between the ages of five and eleven months.

SYMPTOMS AND SIGNS

The earliest symptoms noted are arranged in Table 1. Tenderness of the extremities was by far the most frequent complaint, and the lower extremities were affected thirty-nine times as frequently as the upper. In 15 patients the tenderness had allegedly followed some minor trauma. In 6 cases scurvy was discovered in the course of a routine physical examination in the hospital, and in 1 case the typical roentgen-ray finding was the first noted sign; it was discovered when the patient

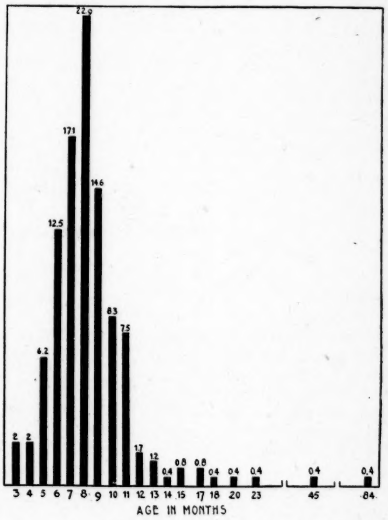

FIGURE 3. *Age Distribution at the Onset of the First Symptom of Scurvy (241 cases).*

The columns represent the percentage incidence in each month of age.

was referrred to the Department of Roentgenology for some other complaint.

The principal physical findings attributable to scurvy noted at the time of the first examination are listed in Table 2. Tenderness in the lower extremities was eleven times more frequent than that in the upper, and swollen lower limbs were observed five times as frequently as swollen upper limbs. Gross

TABLE 1. *The First Symptom or Sign (241 cases).**

SYMPTOM OR SIGN	NO. OF CASES	PERCENTAGE
Tenderness in one or both lower or upper extremities	161	67
Irritability and generalized tenderness†	59	24
Anorexia and failure to gain weight	22	9
Diarrhea or vomiting or both	15	6
Involvement of gums	15	6
Skin rash	3	1
Blood in stool	2	—
Blood in urine	1	—
No specific complaint (scurvy discovered in hospital)	7	3

*In several cases the history contained more than one early symptom, the most frequent combination being irritability and tenderness of one or both lower extremities. This accounts for the fact that the total number of first symptoms exceeds the total number of patients.

†Irritability was present in the history of 107 patients (44 per cent), but it was the earliest symptom in only 59 cases.

blood was present in the stools of 6 patients, whereas in the remaining 2 cases it could be detected only by the guaiac test. Gross hematuria was observed in 1 case, and microscopic hematuria in 3 cases.

The temperature was elevated in 40 per cent of the 228 cases in which it was recorded. In 65 per cent of all febrile cases no associated infection could be demonstrated, the fever apparently being related to the scurvy. An increased susceptibility of scorbutic patients to infection[8] was confirmed in this survey. Thirty patients (12 per cent) had concurrent infections of the upper part of the respiratory tract. This means that the incidence of infection of the upper part of the respiratory tract was at least five times as high in the patients with scurvy as in the total number of all patients admitted to the Outpatient Department over the same period of time. Thirty-one patients (13 per cent) had miliaria, and an equal number had ammoniacal dermatitis. The incidence of rickets was high, this symptom appearing in 22 patients (9 per cent). Anemia was also a relatively frequent finding, 12 per cent of all patients having an appreciable degree of anemia, usually of the hypochromic type. Six patients (2 per cent) had had pertussis at some time before the onset of scorbutic symptoms. Five patients (2 per cent) had definite signs of pneumonia when admitted to the hospital, in addition to frank evidence of scurvy.

TABLE 2. *Physical Signs on First Physical Examination (241 cases).*

PHYSICAL SIGN	NO. OF CASES	PERCENTAGE
Tenderness in one or both lower or upper extremities	199	83
Enlarged costochondral junctions (rosary)	161	67
Involvement of gums	88	36
Swelling of one or both lower or upper extremities	26	11
Petechiae or ecchymoses (excluding ecchymosis of eyelids)	25	10
Ecchymosis of eyelids	8	3
Blood in stool	8	3
Blood in urine	4	2
Exophthalmos	3	1
Tenderness of ribs	2	—
Subconjunctival hemorrhage	1	—
Hemorrhage in retina	1	—
Hematoma (head)	1	—

The following case was particularly interesting in that scurvy simulated pneumonia:

R. S., a 7-month-old boy, was admitted because of a generalized rash and crying for the 3 weeks prior to entry. He had not been receiving adequate amounts of vitamin C. Shortly before entry the gums became swollen and developed purplish areas anteriorly.

Physical examination revealed a well developed and well nourished pale, slightly cyanotic infant lying apathetically, with the legs held in the so-called "frog's leg" position and the right arm outstretched. The temperature was 101°F. The respirations were rapid, shallow and slightly irregular, with occasional cough. A macular rash was present over the anterior thorax, abdomen and lower legs; some of the lesions had brownish crusts, and many were petechial. Both eardrums were full and injected. The upper and lower gums were swollen, spongy and livid, with small petechial hemorrhages visible anteriorly. The pharynx and tonsils were reddened. The lungs contained a few scattered rhonchi. The legs were swollen and tender, and there was considerable beading of the costochondral junctions. The hemoglobin was 49 per cent, the red-cell count 3,460,000, and the white-cell count 15,700, with 75 per cent neutrophils. Blood Wassermann and tuberculin tests were negative, a throat culture was noncontributory, and urine examination was within normal limits. The plasma ascorbic acid level was zero. Roentgen-ray examination of the long bones showed advanced active scurvy.

It was thought that in addition to scurvy the patient had pneumonia, and he was placed in an oxygen tent. Because of the moderate anemia and the patient's acutely ill appearance, blood was transfused the day after entry. In spite of the giving of oxygen, the respirations continued to be rapid and the cyanosis persisted. Roentgenograms showed no evidence of pneumonia, and it was thought that the respiratory difficulty might be a manifestation of the so-called "cardiorespiratory symptom of scurvy" and be exaggerated by excessive pain and tenderness of the ribs. Accordingly, morphine was given in regularly repeated doses. This resulted in prompt relief, including disappearance of the cyanosis.

From 4 to 8 ounces of orange juice was administered daily. No chemotherapy was instituted. The rhinitis persisted and the inflammatory process in the ears did not subside. Paracentesis was done in the 4th week, with release of pus from the right middle ear and the patient was discharged free from symptoms 32 days after entry. During the last week, the temperature remained normal. Roentgenograms of the long bones taken shortly before discharge showed signs of healing scurvy.

ROENTGEN-RAY FINDINGS

In 127 of 133 cases examined roentgenologically, bone changes characteristic of scurvy were found. In 4 cases the changes were minimal but suggestive, whereas in the remaining 2 cases the findings were equivocal.

LABORATORY DATA

In 24 cases fasting plasma vitamin C levels were determined (Fig. 4), and a mean value of 0.087 mg. of ascorbic acid per 100 cc. with a range of 0.0 to 0.3 mg. was found. The mean value for normal infants with adequate nutrition is between 0.8 and 1.4 mg.[4] Although low plasma vitamin C concentration value is a constant finding in untreated scurvy, it is by no means a certain indication of vitamin C depletion.[5] Butler and Cushman's[4] method of analysis of the whole blood and the white cells and platelets is recommended to obtain a more reliable index of vitamin C deficiency.

In 7 patients showing low values of ascorbic acid in the plasma and its absence in the urine, large doses of crystalline ascorbic acid were administered over several days, and vitamin replenishment was accomplished quickly or over a longer period of time, depending primarily on the dose of ascorbic acid employed.*

The serum alkaline phosphatase level was measured in 26 scorbutic patients, and the results were found to be abnormally low. In 1 patient the phosphatase value was 0.19 Kay units (the value for a normal infant of the same age is 0.26 Kay units[7]). The average value in the remaining 25 cases† was

*The details of this study have been reported by Ingalls.[6]

†The results of 18 cases in this series have been published in detail by Shwachman.[8]

3.6 Bodansky units, with a range of 1.1 to 5.8 units, as compared with the mean value for normal infants of 7.2 units and a range of 4.5 to 12.0 units, as determined by Talbot and his associates.[9]

Factors Leading to an Inadequate Vitamin C Intake

Some explanation of the reasons for inadequate intake of ascorbic acid was given in the records of 172 cases (Table 3). In 51 cases, orange juice was omitted because of a rash or gastrointestinal disturbances believed to be ascribable to it, without substituting vitamin C in some other form. In 28 cases, orange juice was boiled or heated or mixed with hot or boiling water. In 1 case, the mother claimed that administration of vitamin C was not recommended while the formula was prescribed. In still another case, a physician had allegedly remarked that the canned foods for babies contained enough ascorbic acid and that additional vitamin C was not necessary. In many cases, the mother claimed that she had been faithfully offering the infant sufficient amounts of orange juice, but further inquiry revealed that in most of them the infant constantly refused it. In 7 cases, however, the informant continued to insist that the child had been receiving adequate quantities of orange juice or ascorbic acid.

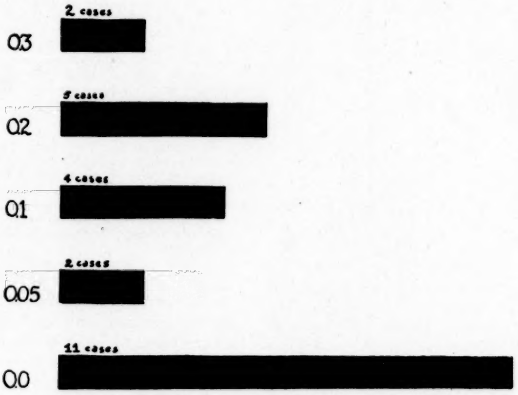

Figure 4. *Plasma Vitamin C Levels in Scurvy (24 cases). The figures represent milligrams of ascorbic acid per 100 cc. of plasma.*

Table 3. *Factors Leading to Vitamin C Deficiency (172 cases).*

Factor	No. of Cases	Percentage
Baby refused orange juice	49	28.4
Orange juice caused gastrointestinal disturbances	37	21.5
Orange juice was boiled or heated or mixed with hot or boiling water	28	16.3
Too small amounts of orange juice were given irregularly	28	16.3
Orange juice caused skin rash	14	8.1
Orange juice unnecessary because "adequate amounts" of vitamin C were given	7	4.0
Orange juice unnecessary because baby "getting enough sunshine"	2	1.2
Orange juice unnecessary because canned tomato juice was given daily in "adequate quantities"	2	1.2
Orange juice unnecessary because older siblings had done well without fruit juices	2	1.2
Orange juice unnecessary because "canned baby foods contain vitamin C"	2	1.2
Oranges were too expensive	1	0.6
Total	172	

All these cases revealed roentgenologic findings characteristic of scurvy. In all, the daily administration of 150 to 200 mg. of ascorbic acid rapidly relieved the patients of their symptoms. The alleged vitamin C intake is summarized in Table 4.

Effect of Treatment

The effect of treatment was recorded in 124 cases. Most of the remaining patients were referred to their own physicians after a diagnosis had been made and vitamin C therapy had been instituted. Relief of symptoms took place rapidly in all the observed cases. Orange juice was administered in

Table 4. *Data Concerning 7 Patients Who Were Allegedly Receiving Sufficient Quantities of Vitamin C.*

Age	Vitamin C Intake According to History
mo.	
8	2 oz. of orange juice daily; not boiled.
6	3 oz. of fresh orange juice daily; not boiled, and no soda added.
10	3 oz. of fresh orange juice daily; all retained.
6	2-3 oz. of orange juice daily
11	25 mg. of ascorbic acid daily
7	3 oz. of orange juice daily
6	2 tablets of ascorbic acid daily during the previous 3 mo.

28 per cent, ascorbic acid in 66 per cent and both in 6 per cent.

* * *

In view of the increasing efforts toward the provision for better health and the supposedly widespread dissemination of nutritional information among present-day mothers, it is surprising that one hospital should have received such a large number of definite cases of scurvy in the last ten years. The incidence in this decade was 41 cases of scurvy per 100,000 outpatient visits, as compared with an incidence of 58 cases during the previous decade. Figure 1 illustrates the steady decrease until 1940, following which a rise occurred during the next five years. The shortage of citrus fruits and their higher cost during the war years may account for this rise. The relative unavailability of physicians during the war years may have been an additional factor.

There is little doubt that mothers of scorbutic children are familiar with the idea of the necessity of vitamin C in the children's diets. The demonstrated frequency of this preventable disease, however, indicates that far more emphasis must be laid on this point in the community. Special stress should be put on the danger of the false sense of security that exists during the rather long latent period between beginning of the deficiency in diet and the onset of symptoms. The following measures are suggested in an attempt to reduce or abolish scurvy in modern communities. First, mothers should be educated by obstetricians and pediatricians concerning the vital need of regular administration of vitamin C in adequate amounts to infants. Second, every physician should question the mother routinely concerning vitamin C intake whenever a child is seen. It is of interest in this regard that extremely few of the babies in this series had not been seen by a physician for some reason before the onset of symptoms. Hence, the fact that the intake of vitamin C was inadequate could have been determined and measures could have been taken to correct the deficiency. Lastly, the public should be educated to accept the cheaper ascorbic acid as a substitite for citrus fruits, whenever the use of the latter is not feasible.

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THE TONIC EFFECTS OF INSULIN IN ACUTE ALCOHOLISM*

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IN all toxic states, the prompt removal of the toxic agent must be the prime consideration in therapy, with the counteracting of its toxic effects and the restoration of impaired organs and their functions as secondary although vital factors. In the treatment of acute alcoholism, rapid elimination of alcohol is important, not only from the point of view of the patient's physical well-being but also for the psychologic implications, in getting him as quickly as possible through the difficult period in which he has not enough alcohol to render him emotionally analgesic, yet too much to permit clear intellectual functioning and satisfactory co-operation. Accordingly, the consideration of means of prompt elimination of alcohol in acute alcoholism has been the subject of much investigation. Attention has focused on the roles of insulin and of glucose, both singly and in combination, on the rate of alcohol oxidation and detoxification.

Chronologically, the consideration of the effects of glucose on the oxidation and detoxification of alcohol preceded that of those of insulin. The difference in effect of alcohol when taken on a full or on an empty stomach has been known to the laity for many years. It was at first assumed that the ingestion of food previous to or simultaneously with that of alcohol reduced the effect of the latter by slowing its absorption. Investigation has shown, however, that the effect is a much more specific one. Thus, Mellanby[1] and later Southgate[2] and others showed that food taken with alcohol reduces the level of blood alcohol; in line with this it was demonstrated that the toxicity of alcohol is in inverse ratio to the blood sugar level.[3] These observations were confirmed and explained by studies showing that glucose speeds the oxidation of alcohol both in vitro[4] and in vivo.[5,6]

With the established intimate relation of insulin to glucose metabolism, it was inevitable that attention should also be given to the effect of insulin on the oxidation and detoxification of alcohol. Results of these studies have shown considerable variance through a voluminous literature, an excellent bibliography of which is given by Clark, Morrissey, Fazekas and Welch.[7] The evidence for the efficacy of insulin, however, is too great to be ignored, and the preponderance of evidence has been on the positive side.[7,8]

Clinically, the tendency has been to use insulin and glucose in combination in speeding the elimination of alcohol. The beneficial clinical results of this form of medication have been incontrovertibly established. This technic was naturally first applied in cases of pathologic intoxication and other acute alcohol toxicities such as delirium tremens and alcoholic hallucinosis. At present it is established as the recognized treatment for this group of disorders.[9] It has, also quite naturally, been extended to use in the milder, relatively uncomplicated cases of acute alcoholic intoxication, in which it has again shown excellent clinical results.[10]

In all this use, the insulin has usually been considered as a secondary factor that acts indirectly by furthering the metabolism of the glucose, which is primarily responsible for the more rapid oxidation of the alcohol, so that, as has been said, "the alcohol burns in the flame of carbohydrate," much as does fat in the treatment of diabetes mellitus. Thus, in the treatment of the more grossly toxic alcoholic states, glucose is given intravenously soon after the insulin, and supplementary carbohydrate by mouth is given subsequently. The same procedure has been used in the simpler states of alcoholic intoxications. Wortis, Bowman and Goldfarb[10] and others, however, have used oral glucose alone in these cases, with equally good results. It has been emphasized, however, that liberal covering of the insulin by glucose is essential and that insulin reactions must be carefully watched for.

It is the purpose of this paper to present the findings in a series of patients with uncomplicated alcoholic intoxication who were treated by being given small doses of insulin, but who were not given the usual coincident liberal amounts of glucose as such.

MATERIAL

The material consisted of 43 patients admitted for acute alcoholic intoxication, of whom 29 were men and 14 women. The duration of the acute alcoholic episode varied from two days to three months. The cases were taken at random and unselected from the group of regular admissions. It may be mentioned that, in comparison with alcoholic patients as a group, all our patients, both those included in this study and those in the control group, were in general in the higher economic and social levels.

METHOD

For some time the customary withdrawal procedure for uncomplicated cases of acute alcoholic intoxication in this hospital has been one of gradual reduction of alcohol, the actual rate of withdrawal

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in each case being determined both by the patient's clinical condition and by a modicum of regard for his comfort, the total period of withdrawal, however, not being permitted to exceed three hospital days or to include more than a certain maximum of alcohol.

The regimen may be summarized as follows. The diet is of high-calorie, high-vitamin type. Fluids are forced, with special emphasis on fruit juices. Liberal supplementary vitamin B_1 is given orally in all cases and intramuscularly or intravenously in those showing signs of vitamin B_1 deficiency — tremors, excessive sweating or any trace of confusion or disorientation — or giving a history of grossly inadequate recent dietary habits. Further medications include some form of antacid for control of gastric and systemic acidity and bitters before each meal as a stimulant to appetite. Physiotherapy and hydrotherapy are included in the daily schedule, together with occupational therapy in graduated amounts. Psychotherapy is given so far as possible, although necessarily in only preliminary and superficial fashion during the actual withdrawal procedure. During the daytime hours, a mixture containing 0.67 gm. of chloral hydrate and 2.0 gm. of bromide compound is given as necessary for restlessness, but not oftener than once in four hours. At night, either 0.1 to 0.3 gm. of pentobarbital sodium or 8 to 20 cc. of paraldehyde is used as a hypnagogue. Whisky is used as the source of alcohol during the reduction period, in doses of 30 cc., not exceeding a maximum allowance of 240 cc. during the first hospital day, 180 cc. during the second and 120 cc. during the third. In this study, the control cases were treated by the above regimen.

The cases in the insulin series differed in their treatment only in the addition of 10 units of insulin subcutaneously twenty minutes before meals two or three times daily and the fortification of the milk or fruit-juice interfeedings with 4 gm. of cane sugar.

During the course of the study the subjective comfort of the patients receiving insulin was so definitely increased that it was believed that the usual supplementary sedation could be drastically reduced, and in the later patients of the series, 10 gm. of bromide compound or 15 mg. of phenobarbital, to a maximum of every four hours, was substituted for the mixture containing chloral hydrate and bromide compound. The significance of this will be referred to in more detail later.

In keeping with the previously mentioned policy of using gradual reduction of alcohol, no attempt was made in this series to withhold alcohol except as in line with the restrictions described heretofore. In a few cases the procedure was to stop whisky abruptly and institute subcutaneous insulin and intravenous glucose in the standard fashion. Patients with delirium tremens, confusion or other states of extreme toxicity, as well as those with marked malnutrition, debilitation, vomiting or intercurrent infection, were likewise treated by abrupt withdrawal of alcohol and use of insulin and glucose. None of the patients who received the combined insulin-glucose therapy are included in this study, either as cases or as controls.

Results

Duration of Withdrawal Period

The comparative durations of the withdrawal period in the 43 insulin-treated cases and in a control series of 564 patients who did not receive insulin were computed. Since the patient is inclined to judge the progress of his withdrawal by days much more than by hours or total amounts of alcohol and to adjust his demands in accord with this concept, comparison of length of withdrawal in terms of hospital days during which whisky was administered was considered to be the best standard of comparison between insulin cases and controls. With the same standard of computation applied to each, the durations may be compared with validity. On this basis, the cases receiving insulin received alcohol for slightly less than half the period required by the control cases, the average duration of the withdrawal periods being 1.0 day and 2.2 days, respectively.

Of equal significance are the comparative figures concerning the number of patients in the two groups who required no whisky subsequent to admission and in whom withdrawal was immediate. Forty-four per cent of the insulin patients received no alcohol whatsoever, as compared with only 14 per cent of the control group.

Ease of Withdrawal

It is obviously impossible to evaluate ease and comfort of withdrawal statistically. It was apparent, however, to both nursing and medical staffs that patients receiving insulin were on the whole more contented and co-operative, less restless and fault-finding and less insistent in their demands for alcohol than were the control patients. This, of course, is borne out by the figures given in the preceding section, since in all the cases, as previously explained, the reduction of the withdrawal period below the three-day limit was more dependent on the patient's comfort and co-operation than on dictum or compulsion. Not infrequently, patients who had formerly been deprived of alcohol without insulin commented on their greater comfort, both physically and emotionally, under the insulin treatment.

Requirement of Sedation

It was observed that with the decrease in restlessness and discomfort under insulin treatment, an appreciably less amount of supplementary sedation was required. As previously mentioned, this was

observed during the course of the study, and the amount of sedative was drastically decreased and in several cases was reduced to zero. The patients treated with a minimum of sedation or none at all did fully as well, however, as did those given the larger amounts. Thus the average period of whisky requirement was 0.9 day in the former and 1.1 days in the latter, whereas it was 2.2 days in the controls. In other words, the speed of withdrawal in both groups was essentially twice that of the controls.

Nutrition and Weight

The comparative average gain in weight during successive weeks of hospitalization was calculated for the 43 insulin-treated cases and for 40 control cases. During the first week, which included the actual withdrawal period, patients treated with insulin gained on an average of 2.0 pounds, as compared with 0.6 pound in the controls. During the second week, the average gains in weight were 1.9 pounds in the insulin cases and 0.5 pound in the controls. During the third week, the average weight gains were 1.1 pounds and 0.4 pound, respectively. Both the insulin-treated patients and the controls were served the same diet, although no patients were forcibly fed on the one hand or refused second servings on the other.

Circulatory Changes

Recordings were made of blood pressures and pulse rates as readily determinable indications of circulatory function. The findings in regard to blood pressure showed no consistent trends. Thus, approximately equal portions of the two groups showed a rise of blood pressure above the admission level by the end of the first week of hospitalization, a fall below the admission level and no appreciable change in blood pressure — that is, difference of less than 5 mm. diastolic and 10 mm. systolic. In general the changes, when they were appreciable, showed approach toward more normal levels. Pulses were characteristically found to be rapid, full and bounding on admission, with a later fall in rate and improvement in quality.

There was no appreciable difference in the two groups.

Insulin Reactions

Among the 43 cases, there were only 3 cases of insulin reaction at a clinical level. Two of these occurred within one hour of the insulin injection, and the third occurred after a lapse of four hours. All the reactions were extremely mild, being characterized by slight perspiration and a feeling of weakness, without changes in pulse rate or blood pressure. They were readily controlled by the administration of 250 cc. of orange juice fortified with 20 gm. of cane sugar. In no case was it necessary to have recourse to intravenous glucose, which, however, was always available.

Comment

The findings described above are of significance not only as demonstrating clinically the effectiveness of the administration of insulin without glucose but also as perhaps shedding some further light on the whole matter of the relation of insulin and glucose to alcohol oxidation. Interpretation of these findings may take one of two main lines.

On the one hand, it may be assumed that the good clinical results are due not to any direct effect of insulin but rather to the effect of glucose already present in the body or derived from the subsequent meal but mobilized by the insulin given. To be sure, the dosage of insulin in this series was relatively small (10 units) and could be covered without too much difficulty by the glucose deriving from the carbohydrate of the subsequent meal. Yet the clinical results demonstrate that whatever amount of insulin was given was of significance. At the same time, the infrequency and mildness of insulin reactions in these cases indicate that the amount of glucose available must be not inconsiderable. Of course, there are the glycogen stores of the liver and muscles, but these are likely to be more or less depleted in the alcoholic patient, and one would hesitate to deplete them further. It appears, however, that dipping into these stores may not be essential to cover any deficit in the food. It has been observed that alcoholic patients show reduced sugar tolerance and high blood-sugar curves, with ready propensity to hyperglycemia and glycosuria.[11] This may be due to the fact that when alcohol and glucose are simultaneously present in the blood, the alcohol tends to be oxidized in preference to glucose.[12] Furthermore, with the usual deficiency of carbohydrate in the diet of the average alcoholic patient, there is a lessening of the usual stimulus for endogenous insulin production, so that for this reason also glucose oxidation is impaired. By the administration of insulin, therefore, as in this series, the metabolism of this otherwise impotent glucose is furthered, and there is a breaking up of the vicious circle in which alcohol directly or indirectly interferes with the metabolism of the element — that is, glucose — that would in turn otherwise speed the elimination of the alcohol itself.

On the other hand, Clark, Morrissey, Fazekas and Welch[7] have shown by experimentation with animal tissues both in vitro and in vivo that in the initial oxidation of alcohol by the liver insulin is in itself an essential factor, apart from glucose. Accordingly, the administration of insulin alone, as in this series, would be of direct significance in the oxidation of the alcohol present without necessarily being entirely dependent on glucose metabolism.

In considering the clinical picture of acute alcoholism and the clinical results of insulin treatment, it must also be borne in mind that alcohol interferes not only with the metabolism of carbohydrate but

also indirectly with the metabolism of proteins and fats, particularly the latter.[6, 13] Thus, re-establishment of normal glucose metabolism also reduces the toxic effects of the intermediate metabolic products of these classes of foodstuffs.

Summary and Conclusions

A series of 43 patients admitted for acute alcoholism were treated by gradual withdrawal of alcohol, with the addition to the control regimen of small doses (10 units) of insulin two or three times daily before meals, without coverage by glucose as such.

The insulin-treated cases as compared with the control group showed the following clinical differences: The average speed of the withdrawal period was twice as great. Three times as many patients neither required nor demanded any whisky after admission. Subjective ease and comfort during the withdrawal period were increased. The requirement of supplementary sedation was greatly reduced, in some cases to zero. The weight gain was increased by threefold, both during the first week of hospitalization and subsequently.

Insulin reactions were rare and mild, being readily controlled by oral sugar.

The coverage of clinically effective doses of insulin by glucose as such is apparently not a vital clinical necessity.

The use of insulin in small doses deserves serious consideration in the treatment of acute alcoholism.

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MEDICAL PROGRESS

DISEASES OF THE VEINS (Concluded)

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BOSTON

Anticoagulant Treatment

The anticoagulants, represented by heparin and dicumarol, have been extensively used in many large clinics, particularly by way of postoperative prophylaxis against thrombosis and embolism. The most significant recent figures come from Swedish sources and from the Circulatory Division of the Mayo Clinic.

As a background for the latest Swedish figures, the second report of Crafoord[28] from Stockholm may be recalled. Heparin was given prophylactically in surgical cases. The earlier method of continuous intravenous drip had been abandoned. The drug was given routinely in four intravenous doses of something like 75 mg. three times during the day, and in a dose of 125 mg. to carry the patient through the night. A series of 325 postoperative cases, in all of which the patients were over forty years of age, was compared with 302 control cases, not heparinized. Among the latter were 33 cases of thrombosis and embolism (11 per cent). Among the heparinized patients no thrombosis or embolism was observed, but there were 3 cases of unexplained fever, suggestive of thrombosis. Outside these series, 40 cases of established thrombosis were treated by heparin, usually with excellent results, but 1 patient actually developed thrombosis and fatal embolism under heparin and died.

Bauer has used a closely similar system of heparin administration, although only for recognized thrombosis. The account of his[29] observations at the Mariestad Hospital, covering the five-year period from October, 1940, to October, 1945, is illuminating. No prophylactic treatment was used, but the staff watched for the earliest local and general signs of thrombosis in the lower leg, believing that 95 per cent of all such processes start in the deep (fibular) veins of the calf. Suggestive signs called for phlebography. If this was negative, no action was taken. If it was positive, 150 mg. of heparin was given intravenously and one or two more doses of the same size were given on the same day at intervals of four

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hours. Then, three daily doses of 100 to 150 mg. each were administered, without any study of the blood. In four or five days the temperature usually returned to normal, local signs in the leg disappeared, and the patient was made ambulatory; after one more day, heparin was withdrawn. The average stay in bed was 4.7 days, and the average total dose of heparin was 1700 mg.

In 209 cases of proved thrombosis so treated there were 3 deaths from embolism, all nonpostoperative, a mortality of 1.4 per cent, as compared with 18 per cent in earlier (control) years. Since heparin was not given until five to seven days after operation, no hemorrhage of consequence occurred. Special advantages of this line of treatment were found to be a greatly shortened convalescence and such a restriction of the thrombotic process that the secondary complications of edema and venous congestion were almost completely absent. The confinement of thrombosis to the lower leg and preservation of the popliteal vein were looked on as decided gains resulting from the treatment, but if phlegmasia alba dolens had developed, the use of heparin, although seemingly effective, did not ward off the late secondary complications.

It will be noted that Bauer does not claim 100 per cent success from this system and makes it clear that its use calls for early and accurate diagnosis. For those who wish to study Bauer's method in detail, his exhaustive paper on the sequels of thrombosis[9] and his account of thrombosis following leg injuries[30] are also available.

Barker, Cromer, Hurn and Waugh[31] have published a report on the use of dicumarol in the prevention of postoperative thrombosis and embolism, based on 1000 cases at the Mayo Clinic. They make a special point of dosage and safe administration. The drug was given routinely, and the prothrombin deficiency was estimated by daily blood tests after the method of Quick. They tried for a prothrombin time of thirty-five seconds (bleeding did not occur if the time was under sixty seconds), which corresponds to 20 per cent of prothrombin in the blood plasma. No fatal pulmonary embolism occurred during the one to three days between the first administration and the establishment of the required prothrombin deficiency. Dicumarol was preceded by temporary administration of heparin and the prothrombin deficiency was maintained for several days to a week after the patients had become ambulatory. Actually, the deficiency might continue for two to ten days after administration had ceased, so that daily tests were kept up until normal levels were reached.

Some patients, most of whom had suffered no thrombosis or embolism, were found to be highly sensitive to dicumarol. In such cases the prothrombin level might fall to less than 10 per cent after the first one or two doses. Bleeding was likeliest to occur in this group and required control by blood transfusion and large intravenous doses of menadione bisulfite (synthetic vitamin K). The doses of dicumarol used were, it seems to me, rather large — 300 mg. on the first day, 200 mg. on the second day and 200 mg. on each succeeding day that the prothrombin in the blood was more than 20 per cent of normal.

The authors hold that even when a thrombus is present, dicumarol will prevent embolism, since old thrombi remain attached to the walls of the veins, and they regard it as the treatment of choice for serious embolism when its source is obscure.

Another instructive account of dicumarol administration comes from Reich, Hahr, Eggers and Lipkin.[32] Both prophylactic treatment (102 surgical cases) and treatment of established thrombosis (33 cases) and embolism (9 cases) were employed. These cases arose among 2591 surgical and obstetric experiences. Uniformly favorable results were secured, and no fatalities resulted. The authors question whether routine use of dicumarol is advisable but are convinced that the drug should be given in all cases in which thrombotic complications are likely to arise, including pelvic operations, intra-abdominal cancer and surgical procedures in patients who have shown a previous tendency to thrombosis. Heparin may properly be given, it is stated, during the latent period before dicumarol produces its effect. Tables of dosage are offered.

In choosing an anticoagulant, one should have in mind the promising method of administering heparin devised by Loewe and his associates.[33] These authors have taken up the Pitkin menstruum, a gelatin-dextrose-acetic acid combination, as a means of delivering heparin to the patient over a prolonged period. They have worked out the required dosage and the appropriate intervals, with and without the aid of vasoconstricting drugs. According to their latest report they had treated 125 cases of thromboembolic disease, 42 of which had already suffered pulmonary embolism. Among these 42 cases were 4 fatalities, which are reported in detail. Clinical improvement, as a rule, was striking. Heparinization, these authors believe, must be continued for ten to fourteen days in uncomplicated phlebothrombosis, but when pulmonary infarction has occurred three or four weeks are required. The full heparin effect must still be present when the patient is first allowed out of bed. Lange and Loewe[34] record further experience with the method in the treatment of experimental human frostbite. It should be noted that earlier trials with the intramuscular injection of heparin itself, as attempted by Walker,[35] had proved that such injections were very painful. Walker also used various menstruums.

De Takats and Fowler,[21] who have previously been quoted as making use of both operative and chemical methods, give an excellent account of the combined heparin-dicumarol sequence, their heparin-

tolerance test and the thromboembolic problem in general.

Thrombosis following leg injuries has been serious enough to call for special treatment by both operative and chemical methods. Allen, Linton and Donaldson[7] speak briefly of prophylactic vein ligation in fractures of the hip. Golodner, Morse and Anguist[36] found that among 86 fatalities in 304 cases of fractured hip, 25 autopsies revealed 9 cases of pulmonary embolism. There may, of course, have been many more, but in any case pulmonary embolism was the most frequent cause of death. These authors recommend prophylactic, bilateral, superficial femoral-vein ligation combined with sympathetic lumbar block, especially for patients who cannot be made ambulant early.

Bauer[9] finds the incidence of thrombosis in leg injuries to be 12 per cent, as compared with 1.6 per cent after surgical operations, 1.0 per cent after childbirth and 2.1 per cent in medical patients. It occurred almost exclusively in the injured leg. He believes that many cases have gone undiagnosed, or at least have not been diagnosed until persistent swelling and pain have called attention to the late stage of the process. Since diagnosis is particularly difficult in the case of fracture, because of plaster casts, splints and other apparatus, he recommends, besides the usual elevation of the foot of the bed and the greatest possible use of the muscles, the routine administration of heparin in the same dosage as in the postoperative group of cases. Under this treatment, he finds a reduction in the mortality from pulmonary embolism in traumatized patients, during three years of trial, to less than one fifth of that previously observed.

Complications of Thrombosis

Bauer's[9] exhaustive monograph on the sequelae of thrombosis deserves detailed study. It is written with the point in mind that since 97 per cent of all obstructive femoral thromboses start in the lower leg, it is most important that early diagnosis be made and that efficient treatment (by heparin) be given to prevent the process from reaching even the popliteal vein. For once an obstructive thrombophlebitis — phlegmasia alba dolens — has become established one must expect that edema of some degree will follow in 100 per cent of the cases. Moreover, indurations, such as often lead to ulcers, are present in 45 per cent at the end of five years, in 72 per cent at the end of ten years and in 91 per cent after a still longer period. Bauer holds that a deficient venous return is always responsible for the edema, and he ignores both lymphatic and vasoconstrictive elements in the edema problem. One must admit the significance of Bauer's figures without fully agreeing with his explanation of postphlebitic edema and induration.

I myself have been interested for years in the postphlebitic leg and have regarded edema as the basic change that leads to so much misery and incapacitation. In a paper read before the New England Surgical Society in 1946 and now in process of publication, I presented an account of the various late complications as I had encountered them in ambulatory patients outside a hospital clinic. (Hospital practice includes an unduly high incidence of ulceration.) Edema was very frequent, induration and ulceration were second in importance, and there were also found many cases of a mild causalgia-like pain complex, of recurrent thrombosis and of venous congestion, including varicosities. It did not seem to me that venous stasis was the whole story. There were late effects resulting from the intense peripheral vasoconstrictions of the acute disease, which could be relieved by sympathetic lumbar block or sympathectomy, and there were cases in which there was present not only a secondary saphenous varicosity but what might be called femoral varicosity as well.

I[37] had previously presented the view that in some postphlebitic states the recanalized femoral vein might be regarded as the source of stasis and back pressure, or even back flow, of venous blood. In selected cases, the femoral vein might be sectioned with satisfactory results, the leg being afterward less heavy and congested. The explanation seemed to be that since the femoral vein was functionally useless, a collateral circulation must necessarily have been established and treatment of the femoral as a varicose vein was therefore entirely logical. In a limited series, these conclusions have proved to be correct, although I cannot see that edema has been favorably influenced by the operation. In some cases I have interrupted the vein at a level higher than the inguinal ligament.

Buxton and Coller,[38] who have taken a similar view, make their second report of postphlebitic femoral-vein ligation. Superficial varices have been sectioned along with the deep veins (femoral or common iliac). Ulcers have as a rule been cured, although the authors are not convinced that the good care given their patients has not contributed more than the operation to the favorable result in some cases. Operations done mainly for edema and fatigue have been disappointing.

My comment is that the postphlebitic state deserves more study than it has hitherto received. Possibly, as Bauer suggests, early restraint of thrombosis by anticoagulants will prevent many of the present-day complications. Once the femoral vein is fully obstructed, surgical attack with thrombectomy may act much like lumbar sympathetic block in doing away with reflex vasoconstriction and its consequences. Should the anticoagulants prove fully as life-saving as operative measures, or actually more so, they will probably be preferred as securing a better postphlebitic leg, for in early cases, at least, they should leave behind a functioning, valved upper and perhaps even lower femoral vein.

As a final word on the thromboembolic problem, I quote parts of two recent editorials, which should of course be read in toto. Allen[39] writes:

> Due to the immensity of the problem in the Massachusetts General Hospital, there has come about a gradual but steady trend toward femoral-vein interruption as an answer to this question. To August 1, 1945, 861 patients in this institution have been subjected to femoral-vein interruption. At first, attempts were made to determine whether or not a thrombus existed, by phlebography — now this method has been abandoned. Early, we learned that the apparent sick leg might be misleading and that often the most dangerous thrombosis was lying dormant in the opposite, apparently normal, side. Therefore, we have gradually become convinced that bilateral interruption should be done. . . .
>
> In this series, there has been no fatality as a result of the procedure. There have been surprisingly few instances of infection or lymphorrhea. Only one of the patients has developed a postphlebitic ulcer. The average hospital stay after femoral-vein interruption has been about six days. Patients operated upon before leg swelling develops have no postoperative edema worthy of note. If the operation is undertaken after bland thrombosis has become inflammatory with pain and swelling, then a period of postoperative edema occurs. . . .
>
> This operation is so safe and so simple and if done on the normal vein produces so little swelling of the extremity, that prophylactic vein interruptions are being done with greater frequency. Up to the date of this writing, this procedure has been carried out in approximately 100 patients in our clinic. All of this group have been elderly patients, who, for reason of their acute disorders, would need a prolonged period of bed rest. Typical of these are the aged with fractures of the hip region.

Allen goes on to allude to the tentative use of dicumarol in his clinic by which fewer operative interruptions may be needed. Coller[40] writes:

> The formation and propagation of thrombi in the vascular tree must be prevented by promoting normal physiologic processes; if the process is initiated it must be stopped. The measures used by the surgeon must be simple, readily available and effective. The treatment of thromboembolism as a complication must neither affect adversely the primary disease nor interfere nor complicate the treatment which is essential to this disease. The morbidity and mortality associated with the accepted therapy must be minimal. When these criteria are fulfilled, the problem of thromboembolism will no longer be a problem.

Obstruction and Thrombosis in Various Veins of the Body

Primary thrombosis of the axillary vein is discussed by Roelsen,[41] who has observed 7 verified cases. He describes the usual swelling, heaviness and congestion of the arm, associated with dilated veins about the shoulder. Apparently these same signs may develop in the absence of actual thrombosis, for obscure reasons. Roelsen finds heparin useful in the acute stages of axillary thrombosis, is opposed to operative interference (resection) except in chronic or recurring disease and advises against immobilization of the arm.

The superior vena caval syndrome is exhaustively described by Hussey, Katz and Yater.[42] Obstruction of the superior vena cava has received renewed attention since phlebography and measurements of venous pressure have become available. The disorder is usually secondary to thoracic tumors and to aortic aneurysm, but may also result from the establishment of a fistula between an aneurysm and the great vein. The symptomatology, according to these authors, is related not only to the caval obstruction itself but to the underlying disease as well. Thus, dilated veins on the neck, chest and arms are frequent, and edema is often present in this same field. Dyspnea and cyanosis could equally well be related to the venous obstruction and to the intrathoracic growth or aneurysm. The authors describe methods of measuring venous pressure and present many striking phlebograms. They call attention to improvement that may result from the irradiation of radiosensitive growths and to the occasional value of surgical exploration.

Elective occlusion and excision of the portal vein is discussed by Brunschwig, Bigelow and Nichols.[43] The matter came up, in their experience, because of injury to the portal vein in the resection of a malignant pancreatic tumor. Finding, in an autopsy on their patient, that gradual occlusion of the mesenteric veins had resulted in many anastomoses with the vena cava, they undertook experimental occlusion of the portal vein in laboratory animals. Omentopexy was found to be useless, but if the portal vein was gradually severed by a loop of linen thread, subsequent resection of the vein was compatible with normal life in 2 of their 4 animals.

Varicose Veins

In my last review, I[1] called attention to publications recognizing the significance of anatomic relations and venous pressures in the etiology and treatment of varicose veins. Possible dangers in the retrograde injection of sclerosing solutions were also considered. Since then, a swing toward increasingly radical operations has become plainly evident, and local anatomic variations in the groin and thigh have again been emphasized.

A thorough study of the saphenous vein and its tributaries near its entrance into the common femoral vein, based on anatomical dissections in 550 cases, is offered by Daseler, Anson, Reimann and Beaton.[44] A great variety of patterns are pictured. With such information in mind, a surgeon can have no excuse for not thoroughly eradicating all connections between the varicose saphenous system and the valveless deep veins in the region of the inguinal ligament and above. I am never tired of pointing out that this, of course, is the chief consideration in the successful treatment of varicose veins.

Sherman's[45] anatomical studies of the connections of the superficial with the deep veins of the thigh have led him to perform a stripping operation, under a general anesthetic, combining this with retrograde injection of a sclerosing solution into the lower saphenous stump, to control the bleeding that might otherwise result from the rather rough eradication of so many saphenous branches. Employing early ambulation, in a considerable series

of cases, he has encountered a minimum of accidents, and reports excellent results.

For Sherman's method of injection and stripping, a system of stripping with actual exposure and section of the large branches as they join the varicose saphenous vein in the thigh might well be substituted — a procedure long used by me in former times and recently advocated by Sapiro.[46] It is probable, however, that Sherman's retrograde injection does not offer the same hazard of penetration of strong solutions through direct perforating veins into the deep system, as is incurred when retrograde catheterization and injection down into the veins of the lower leg are employed. Lyall[47] strongly recommends this retrograde injection (after Pratt's plan) although he notes some disturbing postoperative febrile reactions of considerable severity. (One may well ask whether some of these reactions are not evidence of a deep thrombophlebitis.) Smithy,[48] who also uses Pratt's retrograde catheterization into the veins of the calf, again notes a number of complications, including reactions to the sclerosing agents. My own comment on these observations is to question the value of such retrograde injection. Probably it ensures a little more thorough severance of all possible varicose connections, but considering its occasional undesirable effects and its failure to obliterate permanently the veins it enters (mere thrombosis does not mean obliteration), I question the advisability of its continued use.

It is worthy of note that McPheeters,[49] the exponent par excellence of the injection treatment of varicose veins, writes in favor of saphenofemoral ligation with immediate retrograde injection, stating that "the theory that the preliminary ligation is the first and perhaps the most essential step in the treatment is based on the now proved fact that the flow of blood in any well developed cases of varicose veins is actually reversed" — a matter that he had a large part in demonstrating. He advocates emptying the leg veins by elevating the foot of the table during the operation and, on reversing this position, injecting two thirds of the sclerosing solution into the lower saphenous stump. Thus, he believes that he fills all saphenous tributaries down to the foot. As complications, he cites occasional severe chemical phlebitis and the associated cellulitis following the injections of too large amounts of the sclerosing solution. He has seen cases in which the lower leg and even the thigh were swollen after operation.

For an account of a return nearly to the radical dissections of earlier days one should read Hodge, Grimson and Schiebel's[50] paper on the treatment of varicose veins by stripping, excision and evulsion. A review of the older surgery is given. The authors treated many difficult cases, including postphlebitic varices and those complicated by ulcer. They carried out the usual full dissection in the groin and then removed the varicose veins by stripping and evulsion down to the ankle, making some lower-leg dissections and undercuttings. They applied pressure bandages and used early mobilization. In a fairly short series (195 cases) they encountered no pulmonary embolism.

I have tried here to show how the treatment of varicose veins has swung more than a full circle. Actually, it has gone from injection to Trendelenburg's ligations in the thigh, to radical dissection, including that of the lower leg, then back to injection again, to high ligation plus injection and now to radical dissection. The conscientious surgeon should recognize these cycles and draw conclusions accordingly.

A freakish sort of varicosity is described by Prioleau[51] as originating from the gluteal vein. Such a congenital anomaly is not difficult to identify, but it recalls the hemangiomas, which closely imitate saphenous varicosity. The importance of these lesions lies in the danger of dealing with them surgically. Immediate and late hemorrhage are serious dangers.

The value of venography in the diagnosis and treatment of varicose veins is discussed by Imler, Beaver, and Sheehan.[52] Because they regard varicose veins associated with deep venous obstruction as compensatory, they believe that clinical tests should be supplemented by venography in case the state of the deep circulation is uncertain. Should the deep veins be found obstructed, recurrence after operation for varicose vein must, they say, be expected. Thus, a knowledge of the state of the deep circulation may warn against operation. My comment is that varicose veins do not forward venous blood against gravity. Therefore, a collateral circulation by nonvaricose veins must have been established after a deep thrombophlebitis, if the lower leg is not observed to be grossly congested and cyanotic. If this is true, — and it seems unassailable to me, — obliteration of varicose veins must always be of benefit, regardless of the state of the deep circulation, and need not result in recurrence. Phlebography, however, should give a more complete picture of varicosity in complicated cases than routine tests and should permit a more accurate operation.

Arterial spasm, secondary to ligation and retrograde injection of varicose veins is discussed by Tunick, Nach and Weinkle.[53] These writers studied the resulting arterial constrictions by oscillometry in 50 cases of saphenous varicosity so treated. They agree with DeBakey, Burch and Ochsner's[54] earlier observation that irritation of a venous segment causes reflex arterial spasm. This spasm corresponds in degree to the violence of the local reaction. Clearly it may be very dangerous, in the presence of states of arterial deficiency, and it perhaps accounts for some of the cases of gangrene of a leg that rarely result from varicose-vein operations.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 32321

PRESENTATION OF CASE

A twenty-eight-year-old bipara entered the hospital complaining of pain in the lower abdomen.

About two years before admission attacks of moderately severe, steady, aching, nonradiating, bilateral, lower abdominal pain began, occurring two or three days before each menstrual period and lasting until the end of the flow. Occasional sharp stabbing pains were also noted. Similar episodes of dull aching and sharp twinges in both lower quadrants, varying greatly in intensity and duration, were present intermittently throughout the month. Concomitantly the periods, which had previously occurred regularly every twenty-eight days, became irregular, and the flow became variable, lasting three to seven days. The patient passed many clots and sometimes had cramps at the time of passage. Her condition gradually increased in severity, and during the few months before admission she had lost 18 pounds. Her last menstrual period occurred seven days before admission.

The patient had been healthy except for two attacks of pneumonia in childhood. Catamenia had begun at the age of thirteen years and had always been regular until the present illness, although she had had cramps during the first day or two of the period, until the birth of her first child six years before admission. After her second pregnancy, three years later, she had been told that there was a cyst in the right ovary. Both babies had been delivered at full term by forceps, the second being a breech delivery. The breasts had become slightly tender before each period.

Physical examination showed a young woman who appeared entirely normal except for an irregular pelvic mass in the lower right vault, with a ridge extending across the posterior cul-de-sac behind the upper cervix.

The temperature, pulse and respirations were normal. The blood pressure was 110 systolic, 80 diastolic.

The urine, blood and hemoglobin were normal, and the blood Hinton reaction and a chest x-ray film were negative.

Because of a mild upper respiratory infection, with moderate nasal discharge and a reddened throat, operation was delayed until the seventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR. HOWARD ULFELDER: This patient was a young mother with symptoms referable to a pelvic mass of several years' duration. Although the history and the physical findings increase the likelihood of one diagnosis over others, the results of the studies are not conclusive and merely suggest strong possibilities.

Several points in the history seem to bear on the problem. The patient had been in fairly good health and had had two children, three and six years old. The marital history had been uneventful until the time of the present illness, when both the duration and the interval of the periods became irregular. The history suggests that true menstrual cramps had not been noted until the onset of the present illness, when she noticed bilateral lower abdominal pain that seemed to be worse at the time of the periods. Apparently the symptoms had gradually grown severer, without any abrupt change. The loss of 18 pounds during a few months is noteworthy, but I should like to know more about the appetite and food habits before attempting to evaluate the significance of the weight loss.

Physical examination revealed an irregular mass in the right vault and posterior cul-de-sac. One would like to know whether the physical examination showed evidence of weight loss. One would also like to know the size of the mass and whether it was tender or movable, and whether the uterine fundus and cervix appeared abnormal in any way.

DR. OLIVER COPE: So far as weight loss is concerned, the patient was not conscious of any change in her food habits but realized that her appetite was impaired. She felt generally less well. The physical examination was entirely negative except for the mass in the pelvis, which could be felt behind the cervix, better by rectum than by vagina. The prominent part was more to the right side than to the left. The mass was small, plum-sized, quite hard and, apparently, adherent to the upper part of the cervix or to the lower part of the uterus. The fundus of the uterus was normal in size, was freely movable, and could be distinctly felt, because the patient was quite thin. The mass, which was principally on the right, extended over to the left with a suggestion of irregularity and of diminishing size, disappearing into the left vault. Neither ovary was identifiable, but there was apparently nothing higher up in the vault. The cervix showed minor erosions compatible with two pregnancies.

DR. ULFELDER: Was the mass movable and nontender?

DR. COPE: No; it was fixed and slightly tender.

DR. ULFELDER: Abdominal and chest films, a barium enema, an Aschheim–Zondek test and anything that might give some clue regarding the nature of the palpable mass would be helpful. I believe that only a plain abdominal film and a chest film were really indicated, since surgery was imperative and the risk of operation minimal. Was an abdominal film taken?

DR. COPE: No; it was not. And a barium enema was not given because the mass seemed clearly to be in the posterior cul-de-sac. We doubted whether a barium enema would show anything.

DR. ULFELDER: That was my opinion from the history.

DR. COPE: I also doubt whether a plain abdominal film would have shown anything. An x-ray film of the chest was taken in spite of the negative physical examination, on the principle that in a patient who had lost so much weight tuberculosis should be excluded.

DR. ULFELDER: This lesion must have been of several years' duration. The change in menstrual habit strongly suggests sufficient involvement of both ovaries to interfere with normal ovulatory rhythm. Three diagnoses appear possible in this case: involvement of both ovaries in an ovarian tumor, endometriosis and chronic pelvic inflammatory disease. Nothing in the history supports the last diagnosis. The pregnancies three and six years before admission militate against, although they do not actually exclude, endometriosis. The pain with the periods and the description of the mass, especially in the cul-de-sac, are points in favor of endometriosis. The most probable ovarian tumor in this patient is dermoid, and dermoid is bilateral in about 20 per cent of cases. Mention should also be made of unilateral ovarian tumor, with endocrinologic activity with the production of estrin. Granulosal-cell tumor is the most frequent of such lesions. Tuberculosis must also be excluded.

My diagnosis is endometriosis, in spite of the fact that the patient had recently had children. The likeliest type is endometriosis involving both ovaries and the adnexa in the usual fashion, and I base this diagnosis on the history of pain with the periods and the finding of a fixed mass in the vault extending down into the cul-de-sac.

DR. COPE: Examination under ether revealed nothing beyond what had been observed without anesthesia. We did not definitely identify the ovaries apart from the mass. (I hope Dr. Ulfelder will comment on these findings later.) When we dilated the cervix to see what the endometrium looked like, we could easily look up into the cervix, where there were small, 2-mm. long, firm, polypoid irregularities, which did not bleed easily but were a matter of concern in judgment of what was subsequently done. This was not the usual fleshy type of polypoid mass that eventually extrudes from the cervical canal. The endometrial tissue was whitish, consistent with a postovulatory phase, and was grossly somewhat firm, as if slightly fibrosed, but was considered normal. The uterine cavity was obviously normal, except for the mass that was adherent behind to the upper cervical segment. The lower part of the uterus was lobulated and larger on the right, so that the mass might have been taken for a cervical fibroid, but I did not believe so. On opening the abdominal cavity exploration was negative, except that the tip of the appendix was definitely bulbous, as in a carcinoid appendix — the patient had had no recent attack suggesting a subsiding inflammation. The uterus was normal. Both ovaries and tubes were grossly normal, except for one small area behind the left ovary, which contained a small punctate bluish cyst. On the dome of the bladder on the left side was a puckered area of fibrous scarring, with retraction not more than 1 cm. in diameter containing a half dozen small blue cysts. This area was later excised and given to Dr. Castleman. That was all the disease, except for the mass in the pelvis, which proved to be the rectum and sigmoid involved in three areas of endometriosis; the upper rectum and sigmoid were puckered and attached firmly to the back of the upper part of the cervix and the lower part of the uterus. From this description it can be seen that we agreed with Dr. Ulfelder's diagnosis.

At first excision of the three areas of endometriosis appeared possible. We divided the peritoneum 0.5 cm. away from the areas of gross endometriosis and began to dissect down the sigmoid in the muscular layer. The first area of endometriosis on the sigmoid was resected easily enough, the second with slightly more difficulty. When the rectum was reached it was clear that the third area could not be resected: the disease had infiltrated so deeply into the muscular wall that it would have been necessary to resect the rectum. More careful inspection of the areas of the sigmoid that had been freed showed that the disease had penetrated into the muscularis. When the muscular layer of the sigmoid was opened two cysts popped out, and deep invasion was unmistakably present. We did not know whether the disease extended to the mucosa itself, but it clearly went deeply into the mucosal layer, and to resect the tissue, a combined resection of the sigmoid and rectum, with a permanent colostomy, would have been necessary. I should like Dr. Ulfelder and others to comment on what they would have done at this stage.

DR. ULFELDER: Such a decision is extremely difficult in a patient under thirty years of age.

DR. COPE: The endometriosis was limited to one area on the left ovary and to one on the bladder that was resectable and localized to the rectum, sigmoid and back of the uterus. The two alternatives were

surgical castration and closure of the incision, with subsequent castration by x-ray.

DR. ULFELDER: My decision in this case would have depended on my evaluation of the patient — whether she wanted more children, and how she would react to the idea of surgical castration. It would make a difference whether the possibility of castration had been discussed before operation.

DR. FRANCIS INGERSOLL: I do not believe that I should have castrated the patient at the time, not knowing the entire story, because endometriosis is known to be slow in development. Many patients whose entire ovarian tissue appears destroyed by endometriosis of both ovaries have later had children with apparent ease. I remember one such patient who has had three children and is again pregnant. The lesion is not malignant and can be checked at any time with x-ray treatment. It therefore seems wise to me to leave the ovaries and see what happens in the future; the status of the disease may not change for years.

DR. BENJAMIN CASTLEMAN: Did this patient show signs of obstruction of the colon?

DR. COPE: No. About one third of the circumference of the sigmoid was involved. That fact entered very decidedly into the decisions in handling the case, because I believed that any extension of the disease would have caused intestinal obstruction. We had made a tentative diagnosis of endometriosis preoperatively and had discussed the possible implications with both the patient and her husband. I was also influenced by the facts that the patient had been examined by competent hands and that the disease had appeared in six months and was considered to be growing rapidly, and I believed that intestinal involvement had something to do with the weight loss. In other words, we were dealing with a rapidly progressing lesion whose major involvement was in the gastrointestinal tract. The patient had two children and desired no others. Both husband and wife were reconciled to the idea of castration if that proved necessary. We therefore decided on castration, and we resected the ovaries rather than waiting for additional information. In fact, we thought that the disease had progressed to the point of requiring castration by one method or another.

Dr. Ingersoll's point is well taken, but I was not sure that another pregnancy would occur. The patient faced a very disagreeable time whichever decision we made. I hate to castrate anybody, particularly a woman of her age. But it seemed worse to allow her to face a permanent colostomy. How soon can the patient be safely relieved of the disagreeable symptoms of the menopause by partial replacement therapy? It seems obvious that adequate replacement therapy is contraindicated because the endometriosis would be stimulated to a tumorous growth. Can enough replacement therapy be given to help the patient through the uncomfortable period after acute menopause?

DR. ULFELDER: I believe that symptoms would flare up again regardless of what was done.

DR. INGERSOLL: Theoretically, the symptoms could be exacerbated by estrin, which could, however, be used for temporary improvement and control of the hot flashes.

CLINICAL DIAGNOSIS

Endometriosis.

DR. ULFELDER'S DIAGNOSIS

Endometriosis.

ANATOMICAL DIAGNOSIS

Endometriosis of sigmoid, rectum, bladder and left ovary.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The material we received showed a tiny area of endometriosis on the back of the left ovary, and none on the right. The biopsy specimen that Dr. Cope took from the dome of the bladder and sigmoid also showed endometriosis. Dr. Cope's point about involvement of the sigmoid is important because resection of the sigmoid has been necessary in almost all the cases with involvement of the sigmoid that have been seen in this hospital. I do not believe that x-ray treatment would have relieved the obstruction, once the scarring had gone so far as to produce obstruction of the sigmoid. Resection of the sigmoid would have been necessary.

DR. COPE: That point is worth emphasizing. We thought that the intestinal lesion was potentially malignant and that extreme measures were required from an endocrinologic point of view. The disease, of course, was not malignant, but its distribution was.

CASE 32322

PRESENTATION OF CASE

A forty-five-year-old housewife entered the hospital because of postprandial pain.

About two years before admission the patient first noticed attacks of stomach pain that occurred one or two hours after eating. The pains became progressively worse, and nausea and vomiting developed. Prescribed medication and diets gave no relief. X-ray studies seven months before admission were said to have shown an ulcer. During the illness the patient had lost 45 pounds, but she had regained some weight in the last few months, apparently as the result of marked symptomatic relief obtained from a new regime of diet and medication.

Four years before admission a hysterectomy had been performed for fibroids.

Physical examination revealed little except tenderness in the epigastrium, without spasm or a mass. The tongue was heavily fissured, with smooth red edges.

The temperature was 98.6°F., the pulse 100, and the respirations 24. The blood pressure was 130 systolic, 80 diastolic.

The hemoglobin was 12.5 gm. per 100 cc. The urine had a specific gravity of 1.018 and gave a + test for albumin. The serum protein was 5.9 gm. per 100 cc. A gastrointestinal series revealed a large ulcer crater on the lesser curvature of the stomach midway between the cardia and angulus, which measured 3.5 cm. at the base and was surrounded by a wide collar of edema. The remaining portion of the stomach and the intestines were normal. Gastric analysis yielded 120 cc. of fluid with 7 units of free hydrochloride after fasting, 48 cc. with 23 units after alcohol and 130 cc. with 57 units after histamine.

The patient was maintained on a medical regime for a month, during which she gained weight and was subjectively improved. Re-examination of the stomach by x-ray showed the lesion to be unchanged.

An operation was performed on the forty-third hospital day.

Differential Diagnosis

Dr. Wade Volwiler: Two years' duration of ulcer symptoms in no way rules out the presence of a slowly growing neoplasm, for in many authenticated cases the patients have had symptoms for several years. The initial regime of diet and medication in the case under discussion gave imperfect relief of ulcer pain, and nausea with vomiting was a prominent feature. These symptoms are somewhat suggestive of gastric cancer. It is probable that the weight loss was due to simple starvation from anorexia and vomiting, rather than to the presence of widespread neoplasm. The tongue abnormalities suggest a prolonged inadequate diet.

The large size of the ulcer crater is statistically somewhat in favor of cancer, but statistics are not of great aid in single cases. I am not furnished with the necessary information relative to the peristaltic activity in the ulcer area, and to the presence or absence of rigidity of the gastric wall. I should like to know if the contour of the ulcer crater was perfectly smooth. The presence of free hydrochloric acid does not rule out cancer. Although the patient gained weight and had less discomfort, the ulcer crater did not change in size during a full month's careful observation under hospital conditions. Even very large benign ulcers should show some diminution in size during this interval on a proper therapeutic program. It is possible that expert gastroscopy early in the hospital stay would have prevented a month's operative delay if neoplasm were actually present.

The choice of an exact diagnosis in this case is not possible. The important fact is that the ulcer did not change during a month's ideal regime, and therefore surgical extirpation was properly decided on and accomplished. The information is about equally divided in favor of a malignant and a benign lesion. If malignant, this was probably a slowly growing carcinoma; similar ulceration in a lymphoma occurs in this area, but is infrequent. Since I must make a choice, I shall cast my vote in favor of a gastric carcinoma.

Clinical Diagnosis

Carcinoma of stomach?
Gastric ulcer?

Dr. Volwiler's Diagnosis

Carcinoma of stomach.

Anatomical Diagnosis

Benign gastric ulcer, with penetration into pancreas.

Pathological Discussion

Dr. Tracy B. Mallory: The first impression of the roentgenologist who examined this patient and also of the clinician on the ward was that they were dealing with a benign ulcer. It was decided to give the patient a therapeutic test of three weeks of adequate medical and dietary treatment. When this failed to produce any sign of improvement in the lesion, their confidence was shaken and they began to fear that it must be carcinoma. For this reason operation was undertaken.

On exploration a large ulcer was found on the lesser curvature, which was densely adherent to the pancreas. It proved impossible to separate the stomach from the pancreas, and a portion of the pancreas was therefore resected along with about two thirds of the stomach. It was fortunately possible to do this without interfering with the splenic vessels. The resected specimen showed a sharply punched-out ulcer crater measuring 3 cm. in diameter. The base of the ulcer was formed by pancreatic tissue. Numerous sections from the walls of the ulcer showed no evidence of cancer.

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STUDY OF CHILD HEALTH SERVICES

The medical profession has been well informed through editorials in the *Journal* and the *Journal of the American Medical Association* and through the public press of the Study of Child Health Services. It warrants reiterating that the study is being conducted not only by the members of the American Academy of Pediatrics but by all pediatricians, who, in co-operation with physicians and dentists, are applying a technic to evaluate medical service in one large segment of the profession. It is hoped that this and the recent study of the Commission on Hospital Care will be supplemented by other similar investigations in order that all facts on which physicians can intelligently plan a better and more equitably distributed form of medical care will be available.

To date, the progress of the Study has been most encouraging. Throughout the country most of the state programs are being promulgated by experienced physicians who have returned from the war realizing that a new order is in the offing. Before resuming their former activities, they have been challenged by this opportunity to take inventory of one part of medical practice.

The Study may now be said to have been completely organized. Programs are under way in all the states, and regional conferences have been planned for the early fall to consider the form that national and state reports should take. Substantial funds, largely from voluntary sources, have permitted the work to be carried on with the proper perspective for a work of national proportions. In New England, substantial contributions have been made by the National Foundation for Infantile Paralysis, and in Massachusetts, by the newly formed Bay State Society for the Crippled and Handicapped. In all the New England states, the project is not only launched but well afloat. Rhode Island has practically completed its part in the survey. A pilot study, already finished in North Carolina, has clearly shown that physicians busy in practice regard this as something more than just another survey and that pediatricians consider it a serious responsibility.

The national committee is now considering how to make the best use of material from the questionnaires. In the near future, it will be possible to announce the statistical methods that will be adopted. Although it is clear that many already know deficiencies in medical care will be re-emphasized, it is expected that new light will be shed on the amount of service contributed by practitioners of medicine and dentistry, on the quality of service available in clinics and institutions and on the actual scope of present pediatric practice. All these data should form a basis for future concerted action on the part of pediatricians to improve and extend present health services to children.

Already important side lights of the Study have been observed. It is making legislators reluctant to advance new panaceas for the improvement of medical care until the questionnaires are processed. Furthermore, a great awareness of the importance

of child care is being created throughout the United States. Finally, it has shown that the only way for federal agencies to understand the problems of medical practice is to work with physicians.

DEMEROL IS HABIT FORMING

In a letter to the editor of the *Journal of the American Medical Association*,* H. J. Anslinger, Federal Commissioner of Narcotics, calls attention to the work of experts of the United States Public Health Service and others who brought forth convincing evidence of the habit-forming properties of Demerol. He also refers to the article by Paul de Kruif in the June issue of the *Reader's Digest* entitled "God's Own Medicine — 1946," which appeared under the headline "The pain-fighting power of demerol is as miraculous as that of morphine — without the opiates' danger of addiction."

"This article," Mr. Anslinger points out, "adroitly makes no reference to the work of Dr. C. K. Himmelsbach of the United States Public Health Service and Drs. Hans H. Hecht, Paul H. Noth and F. F. Yonkman of Detroit, all of whom warned of the danger of addiction." "Demerol," he continues, "was placed under federal narcotic control by the Congress because of evidence given before that body of its dangerous properties. Some of the persons referred to in de Kruif's articles could have attended the hearings before the Ways and Means Committee and have testified as to what they thought about the drug, but they elected to remain silent."

Time and again, the general public has been treated to great "scoops" in newspaper and magazine articles by enthusiastic writers of popular science and medicine. Most successful among such writers have been those who dramatize the great advances in medicine, and their writings have proved extremely remunerative. It seems likely that they are often encouraged by the sales-promotion divisions of manufacturers, particularly those of companies that hold patent rights to the remedies in question.

Usually such articles, when properly written and carefully edited, serve the useful purpose of educating the public concerning what they may expect from the medical profession. At times they also serve to stimulate the laggard physician to keep up with medical progress. Careful editing by scrupulous, well informed and critical medical authorities is, however, quite essential to assure that the public learns only established facts and is not treated to half-truths or to unwarranted or premature deductions based on enthusiastic interpretations of preliminary observations or of limited and uncontrolled studies.

Unfortunately the urge to scoop or to be sensational has often resulted in the substitution of drama for truth, and popular appeal has often been placed ahead of the public good. Readers are presented with half-truths or with what they want to hear rather than with the unadulterated facts concerning what has actually become available: the favorable aspects of discoveries are emphasized, whereas their limitations and their possibilities for harm are all too frequently ignored or minimized.

When a new discovery in medicine concerns an item of vanity, such as a cure for baldness or for gray hair, the medical profession should be interested chiefly in ascertaining that the possibilities for harm have not been overlooked. That is particularly true, for example, of the many remedies for obesity and the so-called "rejuvenators," which have been heralded with enthusiasm by popular writers.

Great harm may also be done by giving false hopes to the poor sufferers of incurable disease or by encouraging those who require prolonged observation and care with hopes for a rapid cure when such is not actually the case. These misconceptions on the part of patients often serve to break their morale and also to destroy confidence in their physicians, which often plays such an important role in their general welfare.

In the case of Demerol, the danger is quite clearly brought out by Mr. Anslinger. Patients having pain will insist on relief by "God's own medicine," with the *Reader's Digest's* assurance that it is without danger of addiction. Those already addicted to narcotics are also in great danger of substituting one addiction for another. This may prove quite profitable to those who control the German patents on Demerol, but it may turn out to be quite disappointing to the honest physician who is trying to help rid his pa-

*Correspondence. Addiction to Demerol and *Reader's Digest*. *J. A. M. A.* 131:937, 1946.

tient of his affliction. The danger arising out of de Kruif's article is best brought out by Commissioner Anslinger's own words:

> I fear a wave of Demerol addiction if physicians who read this article believe what I consider the reckless and dangerous statements made by de Kruif that the drug is free from addiction properties. This is information somewhat similar to that which appears in the circular distributed by the manufacturer of Demerol to push sales. Had this article been prepared on a strictly scientific basis, it would have sounded a strong warning about the danger of addiction. Our files contain numerous cases of addiction involving the use of Demerol. I cannot too strongly warn the members of your association about the danger of addiction to Demerol.

The *Reader's Digest* is not noted for retracting erroneous statements that appear in its articles. It might do well to start now by publishing Mr. Anslinger's letter prominently in a subsequent issue.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

CHASE — Harrison A. Chase, M.D., of Brockton, died July 23. He was in his sixty-ninth year.

Dr. Chase received his degree from Harvard Medical School in 1905. He was a member of the American College of Physicians and a fellow of the American Medical Association.

DJERF — Frederick J. Djerf, M.D., of Fitchburg, died July 15. He was in his forty-fifth year.

Dr. Djerf received his degree from Tufts College Medical School in 1929. He was a member of the New England Obstetrical and Gynecological Society and the American College of Surgeons.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JUNE, 1946

RÉSUMÉ

Diseases	June 1946	June 1945	Seven-Year Median
Anterior poliomyelitis	0	2	2
Chancroid	1	1	*
Chicken pox	1401	1282	1170
Diphtheria	21	15	7
Dog bite	1345	1266	1299
Dysentery, bacillary	2	1	2
German measles	570	139	199
Gonorrhea	326	378	378
Granuloma inguinale	0	0	*
Lymphogranuloma venereum	2	1	*
Malaria	56	92	1
Measles	7879	1409	3918
Meningitis, meningococcal	4	17	16
Meningitis, Pfeiffer-bacillus	0	2	1
Meningitis, pneumococcal	2	5	4†
Meningitis, staphylococcal	0	0	0†
Meningitis, streptococcal	1	2	0†
Meningitis, other forms	0	1	2†
Meningitis, undetermined	7	4	5†
Mumps	538	1677	966
Pneumonia, lobar	63	140	215
Salmonella infections	37	18	8
Scarlet fever	425	948	791
Syphilis	373	335	417
Tuberculosis, pulmonary	205	192	275
Tuberculosis, other forms	12	13	23
Typhoid fever	3	2	7
Undulant fever	3	6	5
Whooping cough	517	560	560

*Made reportable December, 1943.

†Four-year average.

COMMENT

Diseases reported at an incidence above the seven-year median included chicken pox, diphtheria, German measles and measles.

Measles was reported at a record high for the month of June but had decreased from the peak of 11,501 cases reported in May.

Diseases reported below the median included poliomyelitis, meningococcal meningitis, mumps, lobar pneumonia, scarlet fever and whooping cough.

Lobar pneumonia was again at a record low for the fifth successive month.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Diphtheria was reported from: Boston, 6; Brookline, 2; Chelsea, 2; Gloucester, 2; Lancaster, 1; Lowell, 2; Somerville, 1; Taunton, 4; Worcester, 1; total, 21.

Dysentery, bacillary, was reported from: Lexington, 2; total, 2.

Encephalitis, infectious, was reported from: Worcester, 1; total, 1.

Hookworm was reported from: Wellesley, 1; total, 1.

Malaria was reported from: Belmont, 1; Boston, 15; Brockton, 1; Chicopee, 1; Clinton, 1; Dedham, 2; Douglas, 1; Easthampton, 1; Everett, 1; Fitchburg, 2; Foxboro, 1; Greenfield, 1; Haverhill, 1; Hingham, 1; Lawrence, 2; Lunenburg, 1; Lynn, 2; Malden, 1; Marlboro, 1; Medford, 2; Merrimac, 1; Montague, 1; New Bedford, 1; Newton, 1; Oxford, 1; Salem, 1; Saugus, 1; Salisbury, 1; Springfield, 3; Stoneham, 1; Taunton, 1; Warren, 1; Watertown, 1; Worcester, 2; total, 56.

Meningitis, meningococcal, was reported from: Brockton, 1; Malden, 1; Newton, 1; Watertown, 1; total, 4.

Meningitis, Pfeiffer-bacillus, was reported from: Springfield, 1; total, 1.

Meningitis, pneumococcal, was reported from: Fall River, 1; Mattapoisett, 1; total, 2.

Meningitis, streptococcal, was reported from: Springfield, 1; total, 1.

Meningitis, undetermined, was reported from: Belmont, 1; Haverhill, 1; Marblehead, 1; Millbury, 1; Saugus, 1; Weymouth, 1; Worcester, 1; total, 7.

Psittacosis was reported from: Cambridge, 1; total, 1.

Salmonella infections were reported from: Boston, 1; Cambridge, 4; Chelsea, 3; Lexington, 1; Lynn, 5; Malden, 4; Newton, 3; South Hadley, 1; Springfield, 1; Swampscott, 2; Winthrop, 9; Worcester, 3; total, 37.

Septic sore throat was reported from: Amesbury, 1; Boston, 3; Mansfield, 1; total, 5.

Tetanus was reported from: Methuen, 1; Pittsfield, 1; Quincy, 1; total, 3.

Trichinosis was reported from: Boston, 2; total, 2.

Typhoid fever was reported from: Lowell, 1; Somerville, 1; Worcester, 1; total, 3.

Undulant fever was reported from: Boston, 1; Hanson, 1; Haverhill, 1; total, 3.

CORRESPONDENCE

BOOKS FOR DEVASTATED LIBRARIES

To the Editor: During the war, the libraries of half the world were destroyed by the impact of battle and in the fires of hate and fanaticism. Where they were spared physical damage, they were impoverished by isolation. There is an urgent need — now — for the printed materials which are basic to the reconstruction of devastated areas and which can help to remove the intellectual blackout of Europe and the Orient.

The need is so urgent, scientists working in Europe are so handicapped, that surely those of us working near well equipped libraries will be willing to sacrifice the convenience of an "office copy" in order to provide library facilities for less fortunate colleagues.

There is need for a pooling of resources, for co-ordinated action so that the devastated libraries of the world may be restocked so far as possible. The American Book Center for War Devastated Libraries, Incorporated, has come into being to meet this need. It is a program that is born of the

combined interests of library and educational organizations, of government agencies and of many other official and non-official bodies in the United States.

The American Book Center is collecting and is shipping abroad scholarly books and periodicals which will be useful in research and necessary in the physical, economic, social and industrial rehabilitation and reconstruction of Europe and the Far East. The Center cannot purchase books and periodicals; it must depend on gifts from individuals, institutions and organizations.

Medical and scientific books and periodicals constitute the most important type of material needed and it is needed *now*. We feel sure that members of the Massachusetts Medical Society and other readers of the *Journal* will want to help their suffering colleagues in war-torn Europe and Asia.

WHAT IS NEEDED: Scholarly books published in the last decade in general science and technology, medicine and the allied sciences, dentistry, chemistry, physics, biography, the social sciences, the fine arts and fiction of distinction. Scholarly scientific books will be especially welcome even if not the last edition of a standard work so long as the book has been published in the last decade. Periodicals in any of the above subjects, including runs of volumes, single volumes and even single issues. Large quantities of the more usual journals are needed, such as *Science*, *Proceedings of the Society of Experimental Biology and Medicine*, *Journal of the American Medical Association*, *Surgery, Gynecology and Obstetrics*, *American Journal of Surgery*, *New England Journal of Medicine*, *New York State Medical Journal*, *Southern Medical Journal*, *Journal of the Association of American Medical Colleges*, *American Journal of Public Health*, *U. S. Public Health Reports Weekly* and journals in the special sciences and clinical specialties. If in doubt, a list of titles available should be sent direct to headquarters before shipping, giving a rough idea of dates and volumes; the inquirer will be informed whether the material offered meets requirements.

WHAT NOT TO SEND: State journals or journals of purely local interest other than those listed above, old transactions of medical societies, material of ephemeral interest, outdated textbooks and monographs, students' compends, annual reports or local state documents, material of doubtful importance published by commercial firms, schoolbooks, books for children or young people, light fiction, material of local interest and popular magazines.

HOW TO SHIP: All shipments should be sent *prepaid* via the cheapest means of transportation to the American Book Center, c/o The Library of Congress, Washington 25, D. C. Although the Center hopes that donors will assume the costs of transportation of their materials to Washington, when this is not possible reimbursement will be made on notification by card or letter of the amount due. The Center *cannot* accept material that is sent transportation collect. Reimbursement cannot be made for packing or other charges beyond actual transportation costs. When possible, periodicals should be tied together by volumes. It will be helpful if missing issues are noted on incomplete volumes. It is hoped that many will feel that they can make part of their contribution the payment of transportation of material as far as Washington.

(MRS.) EILEEN R. CUNNINGHAM, *Chairman*
Division of Medical Literature, American Book Center
Joint Committee on Books for Devastated Libraries
Library of Congress
Washington 25, D. C.

HUNGER EDEMA

To the Editor: In the editorial "Avitaminosis and Hypoproteinemia in Starvation" appearing in the July 4 issue of the *Journal*, reference is made to the reports in the literature of the high incidence of so-called "hunger edema."

I was with an evacuation hospital that took over the Mathausen Concentration Camp in Austria shortly after its liberation in May, 1945. Our experience was slightly different from that reported elsewhere. Edema, regardless of a severe state of nutrition, was rare. We gave these persons plasma, whole blood and fluids. Within a few hours or days edema became intense. Many of the patients who had previously been merely a mass of dehydrated skin and bones developed a marked pitting edema extending over the entire body. Their features were often unrecognizable. Restriction of fluids was necessary to relieve the edema. The blood protein levels before the onset of edema were usually low normal. Under the Germans, the daily fluid intake had been so restricted that edema formation was impossible. Evidence of gross vitamin deficiency was rare, the only picture resembling that of beriberi.

ROY J. POPKIN, M.D.

2007 Wilshire Boulevard
Los Angeles, California

NOTICES

ANNOUNCEMENTS

Dr. John M. Barry announces that he will resume the practice of medicine in association with Dr. Z William Colson at 215 Bay State Building, Lawrence.

Dr. Philip S. Foisie announces the reopening of his office for the practice of surgery at 520 Commonwealth Avenue, Boston.

SEMINAR IN LEGAL MEDICINE

A seminar in legal medicine, sponsored jointly by the Department of Legal Medicine, Harvard Medical School, and the Massachusetts Medico-Legal Society, with the co-operation of the medical schools of Boston University and Tufts College, will be held during the entire week of October 7 to 12. The seminar will cover subjects of particular interest to medical examiners, coroners, pathologists and others interested in medicolegal investigations, and the attendance is limited to twenty. For further information write to Dr. William H. Watters, Harvard Medical School, 25 Shattuck Street, Boston 15.

AMERICAN COLLEGE OF PHYSICIANS

The twenty-eighth annual session of the American College of Physicians will be held from April 28 to May 2, 1947, at Chicago, Illinois. Dr. David P. Barr, of New York City, is president of the College and will be in charge of the program of general sessions and lectures. Dr. LeRoy H. Sloan, of Chicago, has been appointed general chairman and will be in charge of the program of hospital clinics and panels, as well as local arrangements, entertainment and so forth. Mr. Edward R. Loveland, executive secretary of the College, 4200 Pine Street, Philadelphia 4, will have charge of the general management of the session and the technical exhibits.

INDUSTRIAL HEALTH CONGRESS

As previously noted, the Seventh Annual Congress on Industrial Health, sponsored by the Council on Industrial Health of the American Medical Association, will be held in Boston during the week beginning September 30. Headquarters will be at the Copley Plaza Hotel, with some of the meetings scheduled for halls at Harvard University.

Preliminary plans call for meetings of committees and of the Industrial Health Council on September 28 and 29. The first day of the Congress will be given over to a symposium on lead poisoning and to an afternoon surgical conference. A state-society dinner and conference will climax the day. On Tuesday, October 1, there will be a morning symposium on problems in industrial medicine as viewed by labor, management and medicine. Elective conferences are planned for the afternoon; these will cover industrial physiology, administrative methods, aviation medicine and workmen's compensation. A Pan-American dinner and conference will be held in the evening. The third day will highlight medicine and industry in a physicochemical age, and also the place of physical fitness programs in industry, with the Bureau of Health Education of the American Medical Association contributing interesting data. A public dinner for health and welfare leaders, at which a nationally-known industrial leader will be the speaker, will climax the program.

The Congress this year is being co-sponsored by the Council of the New England State Medical Societies.

(*Notices continued on page xv*)